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Program in the History of the Biological Sciences and Biotechnology

George B. Rathmann, Ph.D.

CHAIRMAN, CEO, AND PRESIDENT OF AMGEN, 1980–1988

Interviews Conducted by
Sally Smith Hughes, Ph.D.
in 2003

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Since 1954 the Regional Oral History Office has been interviewing leading participants in or well-placed witnesses to major events in the development of northern California, the West, and the nation. Oral history is a method of collecting historical information through tape-recorded interviews between a narrator with firsthand knowledge of historically significant events and a well-informed interviewer, with the goal of preserving substantive additions to the historical record. The tape recording is transcribed, lightly edited for continuity and clarity, and reviewed by the interviewee. The corrected manuscript is indexed, bound with photographs and illustrative materials, and placed in The Bancroft Library at the University of California, Berkeley, and in other research collections for scholarly use. Because it is primary material, oral history is not intended to present the final, verified, or complete narrative of events. It is a spoken account, offered by the interviewee in response to questioning, and as such it is reflective, partisan, deeply involved, and irreplaceable.

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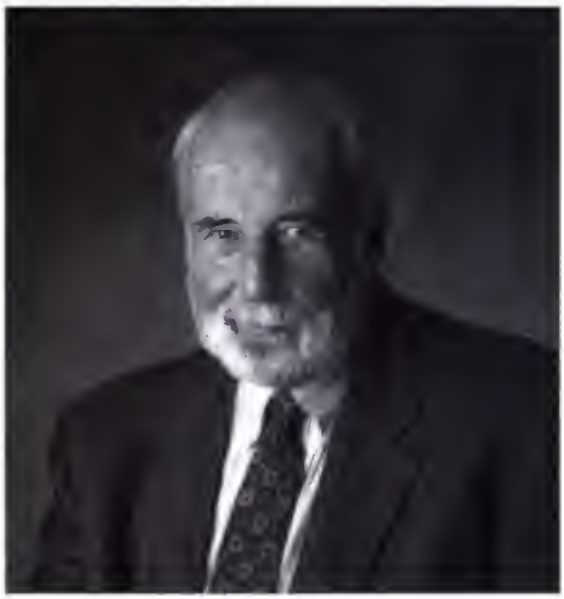

George B. Rathmann

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BIOTECHNOLOGY SERIES HISTORY

Genesis of the Program in the History of the Biological Sciences and Biotechnology

In 1996 The Bancroft Library launched the Program in the History of the Biological Sciences and Biotechnology. Bancroft has strong holdings in the history of the physical sciences--the papers of E.O. Lawrence, Luis Alvarez, Edwin McMillan, and other campus figures in physics and chemistry, as well as a number of related oral histories. Yet, although the university is located next to the greatest concentration of biotechnology companies in the world, Bancroft had no coordinated program to document the industry or its origins in academic biology.

When Charles Faulhaber arrived in 1995 as Bancroft's director, he agreed on the need to establish a Bancroft program to capture and preserve the collective memory and papers of university and corporate scientists and the pioneers who created the biotechnology industry. Documenting and preserving the history of a science and industry which influences virtually every field of the life sciences and generates constant public interest and controversy is vital for a proper understanding of science and business in the late twentieth and early twenty-first centuries.

The Bancroft Library is the ideal location to carry out this historical endeavor. It offers the combination of experienced oral history and archival personnel and technical resources to execute a coordinated oral history and archival program. It has an established oral history series in the biological sciences, an archival division called the History of Science and Technology Program, and the expertise to develop comprehensive records management plans to safeguard the archives of individuals and businesses making significant contributions to molecular biology and biotechnology. It also has longstanding cooperative arrangements with UC San Francisco and Stanford University, the other research universities in the San Francisco Bay Area.

In April 1996, Daniel E. Koshland, Jr. provided seed money for a center at The Bancroft Library for historical research on the biological sciences and biotechnology. And then, in early 2001, the Program in the History of the Biological Sciences and Biotechnology was given great impetus by Genentech's generous pledge to support documentation of the biotechnology industry.

Thanks to these generous gifts, Bancroft has been building an integrated collection of research materials--oral history transcripts, personal papers, and archival collections--related to the history of the biological sciences and biotechnology in university and industry settings. A board composed of distinguished figures in academia and industry advises on the direction of the oral history and archival components. The Program's initial concentration is on the San Francisco Bay Area and northern California. But its ultimate aim is to document the growth of molecular biology as an independent field of the life sciences, and the subsequent revolution which established biotechnology as a key contribution of American science and industry.

Oral History Process

The oral history methodology used in this program is that of the Regional Oral History Office, founded in 1954 and producer of over 2,000 oral histories. The method consists of research in primary and secondary sources; systematic recorded interviews; transcription, light editing by the interviewer, and review and approval by the interviewee; library deposition of bound volumes of transcripts with table of contents, introduction, interview history, and index; cataloging in UC Berkeley and national online library networks; and publicity through ROHO news releases and announcements in scientific, medical, and historical journals and newsletters and via the ROHO and UCSF Library Web pages.

Oral history as a historical technique has been faulted for its reliance on the vagaries of memory, its distance from the events discussed, and its subjectivity. All three criticisms are valid; hence the necessity for using oral history documents in conjunction with other sources in order to reach a reasonable historical interpretation.[1] Yet these acknowledged weaknesses of oral history, particularly its subjectivity, are also its strength. Often individual perspectives provide information unobtainable through more traditional sources. Oral history in skillful hands provides the context in which events occur--the social, political, economic, and institutional forces which shape the course of events. It also places a personal face on history which not only enlivens past events but also helps to explain how individuals affect historical developments.

Emerging Themes

Although the oral history program is still in its initial phase, several themes are emerging. One is "technology transfer," the complicated process by which scientific discovery moves from the university laboratory to industry where it contributes to the manufacture of commercial products. The oral histories show that this trajectory is seldom a linear process, but rather is influenced by institutional and personal relationships, financial and political climate, and so on.

Another theme is the importance of personality in the conduct of science and business. These oral histories testify to the fact that who you are, what you have and have not achieved, whom you know, and how you relate have repercussions for the success or failure of an enterprise, whether scientific or commercial. Oral history is probably better than any other methodology for documenting these personal dimensions of history. Its vivid descriptions of personalities and events not only make history vital and engaging, but also contribute to an understanding of why circumstances occurred in the manner they did.

Molecular biology and biotechnology are fields with high scientific and commercial stakes. As one might expect, the oral histories reveal the complex interweaving of scientific, business, social, and personal factors shaping these fields. The expectation is that the oral histories will serve as fertile ground for research by present and future scholars interested in any number of different aspects of this rich and fascinating history.

Location of the Oral Histories

Copies of the oral histories are available at the Bancroft, UCSF, and UCLA libraries. They also may be purchased at cost through the Regional Oral History Office. Some of the oral histories, with more to come, are available on The Bancroft Library's History of the Biological Sciences and Biotechnology Website: http://bancroft.berkeley.edu/Biotech/.

Sally Smith Hughes, Ph.D.
Historian of Science

Regional Oral History Office
The Bancroft Library
University of California, Berkeley
October 2002

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1. The three criticisms leveled at oral history also apply in many cases to other types of documentary sources.

July 2004

ORAL HISTORIES ON BIOTECHNOLOGY

Program in the History of the Biological Sciences and Biotechnology
Regional Oral History Office, The Bancroft Library
University of California, Berkeley

Paul Berg, Ph.D., *A Stanford Professor's Career in Biochemistry, Science Politics, and the Biotechnology Industry*, 2000

Mary Betlach, Ph.D., *Early Cloning and Recombinant DNA Technology at Herbert W. Boyer's UCSF Laboratory*, 2002

Herbert W. Boyer, Ph.D., *Recombinant DNA Science at UCSF and Its Commercialization at Genentech*, 2001

Roberto Crea, Ph.D., *DNA Chemistry at the Dawn of Commercial Biotechnology*, 2004

David V. Goeddel, Ph.D., *Scientist at Genentech, CEO at Tularik*, 2003

Herbert L. Heyneker, Ph.D., *Molecular Geneticist at UCSF and Genentech, Entrepreneur in Biotechnology*, 2004

Thomas J. Kiley, *Genentech Legal Counsel and Vice President, 1976-1988, and Entrepreneur*, 2002

Dennis G. Kleid, Ph.D., *Scientist and Patent Agent at Genentech*, 2002

Arthur Kornberg, M.D., *Biochemistry at Stanford, Biotechnology at DNAX*, 1998

Fred A. Middleton, *First Chief Financial Officer at Genentech, 1978-1984*, 2002

Thomas J. Perkins, *Kleiner Perkins, Venture Capital, and the Chairmanship of Genentech, 1976-1995*, 2002

G. Kirk Raab, *CEO at Genentech, 1990-1995*, 2003

George B. Rathmann, Ph.D., *Chairman, CEO, and President of Amgen, 1980–1988*, 2004

Regional Characteristics of Biotechnology in the United States: Perspectives of Three Industry Insiders (Hugh D'Andrade, David Holveck, and Edward Penhoet), 2001

Niels Reimers, *Stanford's Office of Technology Licensing and the Cohen/Boyer Cloning Patents*, 1998

William J. Rutter, Ph.D., *The Department of Biochemistry and the Molecular Approach to Biomedicine at the University of California, San Francisco*, volume I, 1998

Richard Scheller, Ph.D., *Conducting Research in Academia, Directing Research at Genentech*, 2002

Robert A. Swanson, *Co-founder, CEO, and Chairman of Genentech, 1976-1996*, 2001

Daniel G. Yansura, Ph.D., *Senior Scientist at Genentech*, 2002

Oral histories in process:

Moshe Alafi
Brook Byers
Ronald Cape
Stanley N. Cohen
Donald Glaser
Irving Johnson
Daniel E. Koshland, Jr.
Lawrence Lasky
Arthur Levinson
Diane Pennica
Steven Rosenberg
William J. Rutter, volume II
Axel Ullrich
Mickey Urdea
Pablo Valenzuela
Keith R. Yamamoto

INTERVIEW HISTORY—George Rathmann

In the biotechnology industry the one figure who garners near-universal respect is George Rathmann. The fact that during his tenure (1980-1988) as chairman, CEO, and president of Amgen, the company became the largest and most successful in the biotechnology industry supports his reputation. But it is the combination of personal qualities and business and science acumen that lift him above his peers. Dubbed by the industry "The Golden Throat" for his smooth delivery, he is also known for his high principles and sound judgment. Rathmann's love and understanding of science shine through in this oral history. But it was his ability to team science with solid business sense that in large part account for the success of Amgen.

This oral history focuses on Amgen in its foundational days. Although Rathmann was not a company founder—the scientific advisory board was in place before his arrival in 1980—he was its first CEO and a firm proponent of the industrial application of recombinant DNA. Not surprisingly, the oral history is heavy on detail regarding the organization of Amgen—its scientific advisory board, venture capitalist support, and IPO. But Rathmann also talks about the company's science, which like that of its corporate peers, ranged widely over various fields of application and then focused on biomedicine. He tells how, despite opposition, he sustained the one-man project under Fu Kuen Lin which eventually produced the product known as Epogen, a red blood cell booster, and one of the two products which account for Amgen's financial success. Rathmann also repeatedly alludes to the creative environment at 3M, his first employer after graduate school at Princeton, and a model for the culture he sought to create at Amgen.

Two interviews were conducted on October 9 and October 14, 2003 on the terrace of the Rathmann's condominium apartment in Palo Alto. Joy Rathmann, devoted wife and companion, sat through all of the first interview and some of the second, only rarely interjecting a remark. Dr. Rathmann spoke at length and with passion and excellent recall. He reviewed the transcripts and Mrs. Rathmann entered the changes he called for. The oral history stands as one of the centerpieces in the collection on biotechnology at the Bancroft Library.

The Regional Oral History Office was established in 1954 to augment through tape-recorded memoirs the Library's materials on the history of California and the West. Copies of all interviews are available for research use in The Bancroft Library and in the UCLA Department of Special Collections. The office is under the direction of Richard Cándida Smith, Director, and the administrative direction of Charles B. Faulhaber, James D. Hart Director of The Bancroft Library, University of California, Berkeley. The catalogues of the Regional Oral History Office and many online oral histories can be accessed at http://bancroft.berkeley.edu/ROHO/. Online information about the Program in the History of the Biological Sciences and Biotechnology can be accessed at http://bancroft.berkeley.edu/Biotech/.

Sally Smith Hughes, Ph.D.
Historian of Science

Regional Oral History Office
The Bancroft Library
University of California, Berkeley
July 2004

Regional Oral History Office
Room 486 The Bancroft Library

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Berkeley, California 94720

BIOGRAPHICAL INFORMATION

(Please write clearly. Use black ink.)

Your full name George Blatz Rathmann

Date of birth 12/25/27 Birthplace Milwaukee, Wis.

Father's full name Louis Frank Rathman

Occupation Insurance Birthplace Milwaukee, Wis.

Mother's full name Edna Blatz Rathmann

Occupation Homemaker Birthplace Milwaukee, Wis.

Your spouse/partner Frances Joy Rathmann

Occupation Homemaker Birthplace 4/17/28

Your children James, Margaret, LauraJean, Sally, Richard

Where did you grow up? Milwaukee, WI.

Present community Palo Alto, CA.

Education Northwestern University BS-1948-
Princeton University MA-1950, PhD 1951

Occupation(s) Biotechnology

Areas of expertise Chemistry & Biotechnology

Other interests or activities bridge & golf

Organizations in which you are active BIO

SIGNATURE George B. Rathmann DATE 5/19/04

CURRICULUM VITAE

George B. Rathmann, Ph.D.
Chairman,
Nuvelo, Inc.

Dr. Rathmann joined Nuvelo, Inc. (formerly Hyseq Pharmaceuticals, Inc.) as Chairman, in February 2000. Prior to that, Dr. Rathmann was a founder of ICOS Corporation and served as Chairman of the Board from 1990 until January 2000. While at ICOS, he also served as Chief Executive Officer and President, from September 1991 until June 1999. Prior to ICOS, Dr. Rathmann co-founded Amgen, Inc. in 1980, where he served as a Director until 1993. At Amgen, Dr. Rathmann also served as Chairman of the Board, Chief Executive Officer and President at various times.

Before joining Amgen, Dr. Rathmann was Vice President, Research and Development, Diagnostics Division, of Abbott Laboratories, which he joined in 1975. Also during his professional career, Dr. Rathmann served as President of Litton Medical Systems, Inc. He previously held research and management positions at the 3M Company, over a period of twenty years.

Since 1982, he has served as an Officer and Board Member of the Biotechnology Industry Organization and was Chairman from 1986-1988. Dr. Rathmann is an Officer and Board Member of the National Science and Technology Medals Foundation. He is on the Board of Trustees of the Fred Hutchinson Cancer Research Center and the Keystone Center. Dr. Rathmann is the Chairman of the Board of Directors of Zymogentics Inc and Ceptyr, Inc.

Dr. Rathmann received his B.S. in Physical Chemistry from Northwestern University, and his Ph.D. in Physical Chemistry from Princeton University. He is a member of the National Academy of Engineering, the American Association for the Advancement of Science, and the American Chemical Society.

Dr. Rathmann was the recipient of The Glen T. Seaborg Medal from UCLA, 1995; The Bower Award for Business Leadership, 1997; the Biotechnology Heritage Award, Chemical Heritage Foundation and BIO, 1999; and the Princeton Madison Medal Award.

INTERVIEW 1: OCTOBER 9, 2003
[Tape 1, Side A]

Hughes: You were at Abbott from 1975 to 1980, and your education was in physical chemistry?

Rathmann: Yes.

Hughes: So how did the jump from a chemical background into the medical field happen?

Rathmann: Well, first I was a premed when I was at Northwestern and had intended to go into medicine. They wouldn't admit me when I was eighteen, and that was enough of a blow to me that I decided I would consider a Ph.D. in physical chemistry, and I had an advisor giving me that story. Though I was admitted to medical school finally at the end of my third year at Northwestern [1948], I was hoping to get in at the end of my second year, and that was not successful. So they admitted me at the end of my third year, and I paid my fifty-dollar admission fee, but I never went back. I went to Princeton to get a Ph.D, but the medical interest was there right from the beginning. So it's not something brand new.

Then when I graduated from Princeton [1951], because I had a very stimulating set of courses in polymers, I went in the polymer direction at 3M [Minnesota Mining and Manufacturing Company] rather than the medical direction. I had a lot of knowledge and extreme curiosity about polymers. Those were fairly early days for polymers. Some of the greatest work had just been done in the preceding eight or nine years. The theories had been developed and then the ability to make things like fibers and so on was now at hand, and it hadn't been ten years before. So, there were exciting opportunities in polymers. I had a bunch of different choices at 3M. They offered me a job in the electrical chemical area, and the chemical area, and the polymer area, and I just picked the polymer one. Then I stayed in that field for about ten years.

Hughes: As a young man with a fresh degree, you had the choice of what field you would go into at 3M?

Rathmann: Well, yes, it was a good year for hiring. In other words, they were looking to hire people that year. That was 1951. It hadn't always been that way. There would be up and down years. As we would visit some of these companies, we would find that there were years that they wouldn't hire anybody. But that year DuPont was hiring a lot of people. I had three job offers at DuPont, and I had three different ones at 3M, and I had a job offer from every one but one company. So, it was a good year to be hired.

Hughes: The offers came on the basis of your dissertation work?

Rathmann: No. I was just a warm body, and I was a Ph.D. graduate from Princeton.

Hughes: Oh, I see.

Rathmann: It wasn't that bad, actually. A Ph.D. in physical chemistry has credibility beyond what it deserves. I was immediately pretty popular on the circuit. I actually had solicited 3M. I heard about it through my brother Dick who had a relationship to 3M. He said, "You really ought to look into 3M; it's a great company." When I went there, I was dazzled,

they were doing so many different things, very exciting innovations. And the concept of innovation as a career seemed more attractive than just grinding out science. I loved science, but the fact was that there was a spectacular aspect to 3M. They were doing things like making reflective sheeting on highways. It was brilliant science. How do you figure out how to do that? Then they had dry copying in the form of thermofax. They had many programs when I got there that were very exciting.

One that was intriguing to me was fluorochemicals. I probably never even thought about a molecule that could contain three quarters of its weight in fluorine, before I was exposed to the 3M fluorochemical program. You were creating a whole new class of molecules, and you had no idea what they were going to do. You already had some spectacular results--very low surface tension, very low solubility, very unusual properties. So I went into the fluorochemical part of polymers when I got into 3M, and I sort of forgot about my medical interests. Although a few years later, one part of my responsibility included the biochemistry area of 3M, which was just beginning at the time. Biochemistry was very intriguing to me. I had some responsibility there. About that time [1973], I left to go to Litton [Industries], and that was a bit of a disaster.

After Litton didn't work out, I was down there in the Chicago area, and a couple of mutual friends said that they were really looking for someone in the diagnostic field at Abbott. I had been acquainted with Abbott for years. I actually had some interactions with them when I was with 3M, but this was brand new. It was diagnostics, and I just loved diagnostics. I just thought that was greatest thing, because if you know exactly what's going wrong, you'll be able to fix it a lot easier. Ignorance is not a very good thing. Diagnostics were a big step forward. In fact, I thought about diagnostics quite a bit before I ever got to Abbott, and it seemed to me that that was a very interesting place.

Hughes: Do you think your early interest in medicine started you down the applied track? You could have become a theoretical chemist, for example. Did that ever attract you?

Rathmann: Anything new attracted me. There would be no denying that; that would be truth. The fact is that quantum mechanics and statistical mechanics were very exciting courses, and I had a little taste of them at Northwestern. But at Princeton I got right up to my eyeballs in theoretical science. I loved it; I thought that it was a very exciting field. I had never planned to be a physician. That really wasn't why I did the premed. I had a brother-in-law, Frank Steldt, who did medical research at [Eli] Lilly [& Company], and that was one of the charms I was hoping to grab hold of: that I would be lucky enough to have a job to do medical research. If the way to get there was to have an M.D. and then a Ph.D., that's what I would do. If you get it with the M.D. alone, I would do that. But I knew if you were going to do medical research, you probably wanted to get at least an M.D.

But when I couldn't get into medical school when I was eighteen, I decided that there were alternatives. My advisor urged me to go to Princeton. He was a Princetonian, and he said, "That's just the right place for you." So I went to Princeton in physical chemistry and did not have a medical thesis. I had a thesis on microwaves, and it was a fun thesis, but it had nothing to do with medicine. But when I thought about it later on, I really missed not having a medical dimension to what I was doing. When I got to 3M, the man, Frank Bovey, who was in charge of the work there--I reported to him--left to

go to Bell Labs to do more biologically driven research. It woke me up again to a deep appetite to be involved with the medical side. But I really didn't do much; I got involved a little bit with the biochemistry department at 3M, but I really didn't do much in the direction of medicine until I went to Litton in what was called at that time the Profexray Division. I renamed it Litton Medical Systems while I was the president of that division. It was all medical; it was medical devices and x-ray film. It wasn't medicine in the form of pharmaceuticals at all. We had nothing like that. But I was still mighty turned on by the fact that you're dealing with people and helping sick people get well. That's the fun thing.

Then of course I had trouble with Litton. We were losing money, and I couldn't see my way through ever having a decent job there, so I left and went to Abbott [1975]. Mutual friends told me about Abbott needing a diagnostic head of research. And then later on I was vice president for research and development. But initially, I was just head of research. Now, I wasn't a CEO, like at Litton. One might wonder why you would want to give up a CEO position to be a research head. Well, I had CEO up to the eyeballs. I didn't need anymore of that. Particularly at Litton, you learn the hard way--it's called the Gray Davis effect--that when things don't go well things don't go well, you're it, boy; you did it all. [laughter] You made all the mistakes, and everybody points their finger, and that was what happened to me at Litton. I was dead meat when I was there for one month.

Hughes: Had you walked onto a sinking ship, so to speak, and then gotten blamed?

Rathmann: Yes, it was a sinking ship, and they didn't hesitate. The first week I was there--I hadn't moved yet; I was still up in Minnesota--I got a telex up in Minnesota: "Stop the cash drain. Your division's going to hell." Well, I looked at the numbers, and the cash drain had been going on for years, but it became my job [to stop it]. And that's right. I mean, if you say to the CEO, "Well, this isn't your problem; this is somebody else's problem," they're never going to get it fixed. So that was okay with me. I knew I had to fix it. But I also knew it was beyond me to fix it. I wasn't a turnaround artist. I wasn't a deal-with-disaster artist. What I was probably better at than anybody around was getting new products launched and getting the ideas and getting the people stimulated to want to do new things, and to get them to do it and take risks and push new ideas. There was no hope for that at Litton. We were doing a bailing job from the time I got there.

Hughes: And of course you didn't realize that when you took the job.

Rathmann: Well, there was an extra nice twist to this, and that is, their numbers did not show how bad off they were. They had become very astute at concealing their problems. But they did know them, because they brought them to my attention the first week I was there.

By the way, you learn from things like this. So the lesson that I learned was if I was going to take another job, I wanted to talk to the top man in that organization, and I wanted to hear him tell me how solid the books were, and how solid their planning was and so on.

Hughes: And indeed you did that at Abbott?

Rathmann: At Abbott, the chairman of the board became a very good friend. Later on, we put him on the board of Amgen, by the way.

Hughes: What is his name?

Rathmann: Ted Ledder. He was a wonderful, wonderful human being, so I couldn't miss with Ted Ledder. But it was an interesting thing that I took the time to say, "I want to talk to him about this company." Abbott was telling me that this diagnostic thing had great potential, but I had been there once, and it was a bad, bad problem at Litton, because nothing was what it appeared to be when I walked in the door. They had profits that didn't really exist. They were artificial.

Hughes: Abbott's diagnostic unit was the way it had been described to you?

Rathmann: Oh, yes. Ted Ledder just said, "It would be fun, if you like what you see." And I did it. Of course, some of the best years were after I got there, and things really popped for us in every way. It was a very small activity when I got there. It was the smallest division by far, and later on it became one of the biggest.

Hughes: Thanks partly to you?

Rathmann: Oh, I would have to say so. I think most of the credit should go to Jim Vincent, who was running the division, who had come in with a strong hand and great leadership. But he wouldn't have made it without other people.

Hughes: Who were Abbott's main competitors in diagnostics when you arrived?

Rathmann: Well, at that time there was one key competitor who we thought about every day, and that was Technicon. Technicon had the SMAC machines for doing diagnostics with big, sophisticated machines. Abbott's approach had been sort of back-door diagnostics. They had developed a relationship with Oak Ridge in radiotracers. So their idea was to make kits based on radioactivity, and the radioimmune assay was a standard vehicle for being able to use radio-tagged material to do diagnostics. It had very, very high precision. So, they had gotten it started that way, but it was going nowhere when Jim Vincent came in. In fact, he proved that it was going nowhere, and he had to change the entire structure. So he had to hire several people, and one of them was me, and the idea was that we would try to build the greatest diagnostic company that had ever been. That was his vision, and it was very strong. He was very driven by this, and he believed in it. But it was almost to the point where it was, like really, how sensible is it that we're taking on Technicon, who's so big, and they've got all this technology. They have special technology to make the biggest complicated diagnostics machines possible. We weren't going to make a big complicated diagnostics machine. Well, we were going to get into diagnostics everywhere it looked like we had a spot.

Hughes: The other company was focusing on the radioimmune approach?

Rathmann: No, that was Abbott's approach. When I walked through the door, we said, "What may come after radioimmune assays? What is the next thing?" And I put some speeches and proposals together. Everybody had thought the next technology would be enzyme assays, where you use an enzyme, which also has high amplification, to signal when

you've got a substance or when you don't have it there. And they already decided that that was going to be interesting. Syva, a joint venture between--

Hughes: Syntex.

Rathmann: Syntex and Varian, yes. So Syva was already doing enzyme immunoassays, and they had a very broad patent, so it wasn't so easy to break into that. So it occurred to me that what we really wanted to do was start using fluorescence, because I had some experience with fluorescence at 3M, and I thought, well, let's see if we can't take advantage of the sensitivity of fluorescence detection. I hired Mick Jolley, who had a fluorescence background which provided momentum for our fluorescence program. I brought him over from England, as a matter of fact, and before long we had a brand new fluorescence assay, which cannibalized Syva's business, by the way.

Hughes: Oh, really?

Rathmann: Yes. Syva's business was going twenty, thirty, forty, fifty, sixty, seventy, heading toward a hundred, but they never hit the hundred. But, the fluorescence assays of Abbott hit a hundred million within two years. So we just took their business away from them.

Hughes: Well, I know from reading the Chemical Heritage interviews[1] with you that you thought and presumably still think quite a bit about the innovative atmosphere at 3M. What was it like at Abbott? Could you compare?

Rathmann: Well, it was very interesting. What happened after I came was we ended up with a blend. The approach at Abbott was very rigid. There were actually three different approaches. There was Abbott Labs, the old Abbott Labs, and that had kind of deteriorated into a pharmaceutical activity that was pretty dull and not very exciting, and the people were pretty low key. That's one activity at Abbott. The next one was the diagnostic area where Jim Vincent came in. What he brought was a lot of rigor, and almost so much rigor that you had rigidity. In other words, before you could start a program, you would go through a proposal process that would take days. And then you would have oversight that was deep and thoughtful and everything was always going to be done according to the book. Which, whether you realize it or not, I thought lacked that one dimension that was so important to 3M, which was the innovative dimension. 3M asked people to do whatever they think is the right thing to do, don't tell them what they have to do. Let them try and do something new and different. So we brought that in, and Jim was very receptive. He could see that it broadened our horizons quite a lot.

When I got there, it was very simple: we want a new hepatitis test, and we want a new thyroid test, and we want an instrument to compete with Syva's. That was it. Those were the only things we wanted. Well, that's too restrictive, compared to what we were able to do, and in fact we did. So what we did was we came up with fluorescence. What did that have to do with exactly the way we were supposed to go? Then we came up with not only hepatitis tests but cancer tests, and very big ones. And then we came up with infectious disease tests and other tests for other physiological problems, and so on.

1. Unedited transcripts of interviews with George Rathmann, conducted on September 16 and 17, 1999, by Leo Slater and Arnold Thackray, Chemical Heritage Foundation, Philadelphia, Pennsylvania.

So we actually expanded our horizons, which sounds like you're not really organized and focused. By comparison with the diagnostic activity when I got there, we were unfocused. We were willing to take on anything. But, on the other hand, we were very successful, and Abbott had the resources to push these things.

Hughes: You and Vincent were at the top, right?

Rathmann: He was at the top; I wasn't.

Hughes: You were just under him?

Rathmann: I was the person in charge of R&D.

Hughes: So what's the blend of science and business here, when you're looking at new programs and trying to figure out which direction to go?

Rathmann: Well, I'd had my taste of business when I was CEO of that one subsidiary [Litton Medical Systems], so I wasn't anxious to have a major business responsibility. I really thought the thing that I'm good at, which I learned at 3M, was product development. I could get people fired up to do product development. I could get ideas. Frequently the ideas that I got were simply stimulus, like getting the things started. In the case of fluorescence, I played a more active role, but in every case wherever there was a chance to show an idea, when I could volunteer, I would do it. But I didn't expect those ideas had anywhere near great merit. The ideas were stimulated by the idea that having ideas was a good thing.

When I got [to Abbott], the whole tenor of the place changed from one that was grind it out, grind it out, grind it out, make sure you've got all your details right. Make sure you execute it properly, and all that. I hated the word execution; I liked the word innovation, and I brought that from 3M. The other thing I brought was a multi-product strategy. Whereas it had been very nice before to be able to say, "We just want these three things," I said, "I want everything. I want to look at anything and everything." I looked at the MSR, I guess they were called, the Marketing Survey Reports, and would note any assay of any kind that had now started to look like it was going to work. So, somebody had a new assay for a virus, well, let's take a look at viral assays. Someone had a new assay for therapeutic drugs, so let's consider therapeutic drugs.

Hughes: Did that mean hiring new people with those approaches?

Rathmann: We hired a lot of people while I was there.

Hughes: Because you wouldn't necessarily have virologists, would you?

Rathmann: Well, yes. We actually had one of everything when I got there. But, if you hire biochemists, you can get what you want. Immunology is different from virology which is different from cell biology and all the rest. Then you had a core in some of these areas. But I hired primarily biochemists.

Hughes: One thing I remember reading about Abbott, and it may have been a little after your time. But Abbott's diagnostics became very competitive. They became the company to

beat, would you not say, in the diagnostic field? One of the things I remember reading was that they had very strategically placed machines, free machines in their customers' laboratories.

Rathmann: One of Vincent's first strategies was, despite the fact that we initially only had the ABA 100, that if you could make a machine that everybody wanted, you could sometimes give it to people and then charge them for the consumables. That, by the way, was also a 3M philosophy. You want to sell razor blades, not razors. In fact, if you give away the razor, and you get a lot of razor blade sales, that's all right. You're going to be okay. So, he wanted to do that. Now, the interesting thing was that the machines the division was excited about didn't work out very well. The ADC 500, which was a $300,000 machine, and the MS 2, which was a $70,000 machine, were both disappointments. Of course, Technicon sold expensive machines. So that was kind of a model out there, and that was what you had to do. I didn't like machines at all and never thought we would produce any kind of machine, until what happened when one of the guys came along with a very neat way to do enzyme assays, and that was a very simple machine. We called it the Quantum. We made it for just a couple of thousand dollars, and we gave it away. Vincent said right away, "Oh, this is perfect for us." So, you couldn't give away the $500,000 and $300,000 machines. But the ones that we came up with, yes, you could give them away.

Hughes: And that meant that the customer was obliged to use your product in that machine?

Rathmann: And then you had the wherewithal, once you had a machine, to introduce additional assays for that machine, and you automatically could grow your business without ever putting any more machines out. That machine was now capable of doing as much as $20,000 a year in assays. So, each machine was pulling through $20,000 worth of reagents. That was pretty nice.

Hughes: Do you have any idea why Abbott spawned a number of biotech executives, you of course being one of them? And you mentioned Jim Vincent. We haven't mentioned Kirk Raab. Is there a reason that they came from Abbott?

Rathmann: There were actually two companies in the pharmaceutical industry that furnished more executives than any other, and they were Abbott and Baxter. Abbott and Baxter were very similar. They were just a few miles apart there in Chicago. And they both were a different kind of pharmaceutical company. Neither one had the biggest therapeutic pharmaceuticals. Abbott got into erythromycin very early, but it was not the backbone of the medical work. But diagnostic was a totally different animal; a different kind of pace, a different kind of level of innovation. The people in the pharmaceutical part of Abbott could not comprehend the average diagnostic mindset. They couldn't believe that anybody wanted to work that hard, that aggressively, or that innovatively. I mean, they were really grinding out. So both Baxter and Abbott were a different breed of pharmaceutical company. Now, it's not surprising that biotech would be an attractive place for an executive from a pharmaceutical company, but what is surprising is that they weren't pharmaceutical executives. Not I, not Kirk Raab, not Jim Vincent, and certainly not the people from Baxter. There are about half a dozen out there.

Although in the last five years, major pharmaceutical executives have moved into the biotech industry. I hired one. Bill Rutter hired one. Jim Vincent hired one. As the

biotech industry got big enough and strong enough, it was more attractive, not quite so rag-tag as in the early days. But the fit with the diagnostic mentality was very good, and even the Baxter mentality, which was a much more aggressive type of research and marketing.

Hughes: As I said at the outset, it was 1975 to 1980 that you were at Abbott. That's the time when recombinant DNA was beginning to take off.

Rathmann: Yes.

Hughes: When did you first hear about it?

Rathmann: I know exactly, and I'm not proud of this, because I should have heard about it by reading about Watson and Crick in 1953. I didn't really think about it until the head of the pharmaceutical division, the vice president of pharmaceuticals there, Ira Ringler, who was a close friend--we lived as neighbors out in Barrington Hills--called me up one day, and he said, "George, we're going to take a trip." I said, "Well, why do you want to do that?" He said, "Because there's stuff going on that we need to know a lot more about." His words, not mine. "I want to go out on the West Coast--mostly out on the West Coast," which wasn't true exactly because Boston had its share [of biotech companies]--"Let's go out there and we'll see two or three companies that I've heard about. I just don't know what they're doing and I'm really intrigued, and we ought to just do it." It was kind of like a committee of two for Abbott Labs to see what we could learn.

Hughes: What year was this?

Rathmann: This was about 1978. Recombinant DNA was the subject, of course. And yet, there seemed to be two parts to this industry--recombinant DNA and monoclonal antibodies--and we took on both. We went out and saw Cetus (recombinant DNA) and Hybritech (monoclonal antibodies). We did not see Genentech. We didn't have access to them, and we didn't know that much about it. By '78, Cetus was the oldest biotech company for that time, and they were also the biggest.

Hughes: There weren't very many in 1978. A handful.

Rathmann: Just a handful.

Hughes: Had Dr. Ringler been reading the literature?

Rathmann: He was well informed from the literature and pharmaceutical contacts. Well, there's nothing secret; I could have been reading the literature as well. But I was pretty much buried in what I was doing in diagnostics, [and] I didn't think about therapeutics that much. It was pretty clear that Cetus had some interesting stuff going on. It was very scary, the formidable part of having to work with certain kinds of containments and so on. The fears of recombinant DNA were outlandish.

Hughes: That was the height of it, wasn't it?

Rathmann: I don't know whether they had it when we started in '78, but by '80, Abbott had their own recombinant DNA activities. I got involved in that when I was there. But the first step was Ira and I going out and seeing these companies and realizing that they were--

[Tape 1, Side B]

Rathmann: --and such an immediate potential impact on health care. If you could have antibodies that were so highly specific that they could be used in diagnostics, but they could possibly be used in therapies as well, that was just phenomenal.

Hughes: What other antibody companies were around? Hybritech. Was Genetic Systems around yet?

Rathmann: I think Genetic Systems was around, but I didn't see them.

Hughes: Were they talking therapeutics as well as diagnostics?

Rathmann: The general theme for those that talked antibody companies was, they would start out with antibodies for diagnostics. Then they would have antibodies in therapies somehow, possibly carrying a radioactive tag and getting to a specific, a "magic bullet" is what they were referred to in those days, which would eventually have a broad therapeutic impact. Because it was clear that though Abbott proved diagnostics could be a billion-dollar business, there weren't many people in '78 that thought there was such a thing as a billion-dollar diagnostics industry. But there were plenty of billions of dollars in the therapeutics business. So Centocor, Hybritech, companies like this, all had their sequence worked out. Probably, first of all, diagnostics, and then in vivo diagnostics. For example, I could image your tumor if I administered a radioactively tagged antibody that would seek out the tumor and reveal its location. Most companies visualized in vivo diagnostics would pave the way for therapeutics based on toxin-carrying antibodies that would seek tumors and destroy them (magic bullets).

Hughes: How realistic was that in 1978?

Rathmann: Oh, it was true, but it would take many years.

Hughes: What I mean is, did they have a scientific path? I'm getting way over my head, but I understand that the therapeutic use of monoclonals has not been the easiest road to actually walk.

Rathmann: Well, okay, when you say realistic, in fact, the biggest monoclonal therapeutics were not discovered in the seventies, were not discovered in the eighties, were not discovered until very late in the nineties. I don't know any good explanation for that other than I've watched about a half-dozen cycles like that where the technology is ahead of commercialization by a lot of time. The visionaries see the commercial potential very early, sometimes too early, and eventually everything catches up with it. Antisense, which was so dramatic: take the fundamental property of DNA (two bonded strands), and you're going to use the second strand to turn off a signal from the first one--boy, that was popular stuff with great potential for five or six years before anybody really had a product. In fact, some companies like Gilead were antisense companies, but they spent a lot of time doing everything else, because antisense was so hard.

Hughes: [laughs] Did you recognize that at the outset?

Rathmann: Well, in most cases I went along with the conventional wisdom, which is, this is potentially interesting, but it's ahead of its time.

Hughes: Were these early companies that had to get venture capital and other funding, how much of this was a sell job rather than actually executable?

Rathmann: Well, we always had an expression at 3M that nothing ever got started without a huckster. And I was one of the hucksters. I was not as big of a huckster as some of the other guys. But the huckster was the guy that got you keyed up. He was the guy that predicted early success, frequently when there wasn't one. But without the huckster, you didn't do anything. So this was not viewed as a bad thing by 3M. If somebody got behind something, and they really pushed it too hard or too soon, that's far better than being too late.

Hughes: Did you practice that philosophy at Amgen?

Rathmann: Oh, yes. I always felt that there was a certain downside to being the huckster, and you're now aware that there's a very tempting path. The tempting path is to be visionary, and being able to say to somebody, "You know what we can do with this? We can not only start here, but we can do this and this and this." And by being a visionary, you can convince people that there's a future when they didn't recognize it before. And sometimes you can convince them that there's a future when there isn't a future, as you may sound so real and down to earth. Then, when it is least expected, the idea pays off. Monoclonal antibodies were discovered in 1976, and the biggest successes in therapeutics, which everybody was predicting in the early days, were in the last five years.

Liposomes! I just heard another discussion on liposomes in the last week. Liposomes were a very common item to produce fifteen years ago, and it meant that you can put anything in these little particles, and that was going to be a way to deliver drugs. Well, most of those never did succeed. I've heard, in the last two months, some things that might be possible for liposomes. So they went through a period of great enthusiasm. A liposomes company was formed and other liposome companies were formed, and they never went anywhere because they were ahead of their time. They hadn't figured out exactly how to do all of it.

Hughes: It seems to me from probably Litton on, maybe before that, you were a hybrid. I mean, you were acting as a businessman and as a scientist. For example, when you're predicting the future therapeutic use of monoclonals, obviously there's a business aspect to that, but also you have to have some clue about the science.

Rathmann: Well, 3M training was very interesting because they tried to do really good science. Some people said they never did as good science as at places like Merck. I think that's true. But they also had their eye on the importance that you have to bring money into the company if you're going to continue to do exciting things, and that means sales and that means profits and all the rest. And the profit margins that 3M aspired to were very high. They felt that was very important. They felt that if you wanted to have an efficient company, you had to be very sure that your profitability on any product was very high.

Otherwise, you kind of bleed to death. The product was out there, but you can't bring enough in to sustain its growth. It was very clear at 3M that this then was designed to be pragmatic and practical, though good science was considered pretty important for really being able to get to the important stuff. But you really had to be aware of what the commercial implications were right off the bat. And of course Abbott was much the same. It was driven by the idea of being a more successful diagnostic company than anybody had ever been. And you don't do that by just thinking esoteric things and sitting at a desk all day.

My father was a businessman. I was not embarrassed about the business aspect of the company. So yes, you're right, it was a blend right from the beginning, and when I looked at recombinant DNA, that was the same thing. It's a tremendously exciting technology. I wanted to study the technology. I did not decide to start a business; I decided to study recombinant DNA so I would understand it, because I was going to the people at Abbott to get them to do things that I thought were possible. They would always explain to me why they would cost you an arm and a leg, and it would take you forever. And I thought, well, I've just got to understand this for myself. So when I lined up a relationship with Winston Salser at UCLA, it was to take a leave of absence for six months and learn recombinant DNA.

Hughes: Now, why Winston Salser? How did you know him?

Rathmann: Well, one of the people I'd hired at Abbott was a Ph.D. molecular biologist from Winston's lab. So when I was being frustrated at Abbott that I couldn't get some of the things started in recombinant DNA that I wanted, Phil Whitcome said, "Well, I'll take you out to my old professor, Winston Salser; he can help you on that." And in fact, he could; Phil knew that Winston had a hepatitis clone. What had struck me as being an important thing to do at Abbott was to get away from having to bring in infectious materials in order to have our standards for our diagnostic tests. Our standard positive was derived from infected blood. That meant that everything in that place had to be special-class biohazard containment and all that stuff, and I said, "Gee, the hepatitis surface antigen cannot propagate hepatitis. It's a marker, but it does not carry the disease. But if you isolate it from disease-carrying bugs, then you have to assume that everything is infected. But if you were able to make it by recombinant DNA, the plant would just be simplified beyond belief!" And I said, "We just have got to get it by recombinant DNA." So that's when I tried to turn on the people in the recombinant DNA area at Abbott, which had been going on for about five years, but they wouldn't do anything.

Hughes: What were they afraid of?

Rathmann: Well, the whole field was very new, and the ability to do exactly what you wanted to do hadn't been established yet. So they were quite correct that it might be very complicated to successfully make this stuff. What they were protecting against is taking on a job that might be too hard, take too long, cost too much money or be deemed too dangerous. So they just simply said, "It will cost a million dollars, it will take two years"--

Hughes: So it was considerations like that; it wasn't the fact that there was a controversy raging on the political front?

Rathmann: Well, that was there too, in the sense that because of that, it probably would take two years. In other words, at Abbott they had to respect the idea that everybody is scared to death of this stuff, and therefore the first thing you organize when you organize DNA work is a biohazard committee. "The biosafety committee" would have been a better name, but the biohazard means that you can scare most of the executives in the company any time you want by saying you've got a new question about biohazard in what's going on. What actually occurred as a result of that was an enormous barrier, or I should say barriers, to getting research done. For example, if anybody in the DNA area had a cold, they had to go home because of the risk that you would start to put disease genes into something that could infect human beings and spread new diseases. So anybody with a disease had to go home.

Hughes: Now, was that mandated by the NIH guidelines, or was that Abbott policy?

Rathmann: Companies like Abbott immediately adopted the NIH guidelines, and then they said, "Well, we're going to do better than that. So whatever the NIH guidelines say, we're going to do better." Now if that's your goal, there's no limit. If you say, "I'm going to follow a guideline," that's one thing. If you say, "I'm going to do better," where does better stop? It doesn't stop. And it didn't stop there. There were certain bureaucratic parts of Abbott, the quality assurance head, and the medical head, and so on, oh, they got their hands on this. "Oh, this is lush! I mean, boy, now we're controlling the company. We're going to be more powerful than anybody in the company." And so not only did you have to send somebody home who had a cold, but before he came back into the laboratory, he had to go over to the health department at Abbott and be given a clean bill of health. Now, what eventually happened was that you would see these people lined up outside. If eight people had a cold, and in that group, they had to line up relative to any other people with colds that might have to go to the health department. And it was a terrible burden. Everything you did took extra time. Then you had the review of your protocol, so if you had an idea and you wanted to run an experiment, it had to be submitted to the biohazard committee, and they would ponder this thing. Most of them were not scientific, even though they should have been. I ended up on one biohazard committee, and I tried to say, "Let's get the job done! Let's not stand here and delay one program after another because it might still have some risks. We're never going to get anything done." So that was the problem at Abbott.

Hughes: What did you think about the risk versus benefit issue?

Rathmann: I had no real first-hand sense. I figured I was going to learn it. I was going to find out what the story was by working with Winston in his lab, and I'll find out how risky it is. I didn't know ahead of time, but I do know that when I started with Winston scientifically, I was expecting that I was going to come up the learning curve from square zero.

I never did that because Winston had become involved in starting Amgen. So that's how I got linked to Amgen. Winston said, "Well, I can't really do what I hoped to do with you, to have you as a kind of a sabbatical in my lab, because I'm going to be spending my time starting a company. Now, you can still come and be in my lab, but I'm not going to be able to spend much time with you." Well, that defeats the whole thing. So I said, "I'd just as soon consider what he's planning to do as an area of

interest. What is this Amgen going to be?" Then he gave me a hard sell, that maybe I could be a good guy to come to Amgen. That's how it all started.

But it was clear when we started Amgen, and we had to pick a place to work, that some of the considerations about safety loomed pretty big. For example, there was a business park that we eventually decided to go to, though we looked at a bunch of different places. This business park was on the outskirts of Thousand Oaks, way away from downtown, and we were at UCLA. So it was pretty far out, but it was a pretty area in Thousand Oaks where we picked this business park. When we looked at the business park, there were three buildings that we could have used, two that were really reasonable. Actually, I remember the thinking, because it's so different from what I would think today. That was, the prevailing westerly wind would carry the bugs, whatever you had, the high-risk stuff, to the east. There was a residential area right here, and we didn't lease that building, because it would be butting right up against the residential area, and the risk of things being carried into the residential area was much greater. Well, not really, I mean, another hundred yards, what the heck did that mean? But just the same, it was actually a consideration, and we did not take that space, we took the other space, and then later on we got the space and had stopped worrying. The first decision was being influenced by this uncertainty as what you were going to experience. You did have to say to yourself, "How do you reconcile these tremendous fears?"

For example, at the Abbott program, they bought an electron microscope. Their idea had to do with doing the job right, and that's because some work had been very successful, based on the electron microscope. They were using the electron microscope at Amgen for ten years, so it wasn't a very good choice, because you're taking out a hundred-thousand-dollar cost, a full-time person, for what might not be a very essential step. But it was the way they started. But the important thing that they did at Abbott, which was quite strange, was that they had their laboratories in different places, and they didn't know, they really were wrestling for weeks, with how to transport a specimen from this laboratory to this electron microscope. "How are we going to do that?" It's almost as though people had anticipated the AIDS virus, without knowing that there was such a thing, and assumed that anything you did in recombinant DNA was potentially more lethal than anything you had ever seen before in any disease. The idea was that you were dealing with human genes and human diseases, and all of a sudden, you're going to take a cell like *E. coli*, a bacterial cell, that multiplies like crazy, and it's going to multiply a disease that's lethal to man. And that's what's scary. And a lot of times you can't prove that it's <u>not</u> going to do this until you run the experiment. The thing that escaped, in other words, this bug that you now found out is very dangerous, is flying through the air, and everybody knows that these things are certainly out in the air, around the building. Nobody is silly enough to think that containment really means that none of those bacteria ever survive outside the building.

Hughes: Were the people around you having similar concerns?

Rathmann: Well, the biggest concerns had already been dealt with in Boston. They were dealt with by slowing down the Boston contingent of biotech so that Genentech could beat them. And that's really what happened.

Hughes: You think?

Rathmann: It was not a trivial thing. The mayor of Cambridge [Alfred Vellucci] got on his high horse and decided that he was going to put in more constraints and more restrictions and more regulations than anybody had ever dreamed of and had scared the hell out of everybody. So we all were concerned about that, and we all thought that was overkill, but you didn't know how much you could back away from that overkill. Once you set up a procedure that says you have to do this, this, and this, now you would have to work very hard to prove that it wasn't necessary. You almost got locked in. That's what happened at Abbott. They got locked in. You had levels of containment. I can't remember the term right now.

Hughes: P3 [physical containment 3] labs?

Rathmann: Yes, P3, that's it. So you had P1 and P2 and P3, and then you had P4. Abbott already had a P3 that they were putting in, and they were shooting for a P4, the idea being that if you want to be better than the next guy, you better have a higher containment. Now, the problem is, at P4, you had to put on suits with helmets and everything else. You couldn't move in P4.

Hughes: Well, a P4 lab is at the level of Fort Detrick, isn't it?

Rathmann: Yes, exactly right. And there are times when you need P4. But if you're taking P4 for any piece of DNA of any kind and saying, "Well, I'm playing with DNA, I'm playing with something that potentially could do anything horrible, I need P4." They set up their P4 lab, they really did. They expected that they weren't going to use it. But then people said, "Well, you've got the P4, so you might as well use it." So that just burdened them with a very slow process of trying to get anything done. That plus the biosafety review of every protocol, and they would have to go on an appeal--

Hughes: Wasn't that same system in place everywhere?

Rathmann: Amgen never put in a P3, we didn't put in a P2; we did everything P1.

Hughes: So you're saying that you weren't slowed down in the way the Boston group was?

Rathmann: Well, Genentech had pioneered the West Coast approach.

Hughes: Well, there are other things, at least to my mind, that explain why Genentech won the race for human insulin; and that's that they had a unique technique.

Rathmann: What unique technique?

Hughes: Well, they had the combination of synthetic DNA and recombinant DNA. Isn't that ultimately why they won?

Rathmann: Yes, they won because of synthetic DNA.

Hughes: Did the NIH guidelines and that whole paraphernalia actually slow down research?

Rathmann: Well, it certainly did, but it was still very enlightened. The NIH guidelines, to my mind, you can attribute to them the big success of DNA in the U.S., because it gave people the

comfort level they needed, and you didn't have questioning every day, every experiment, every hour if you stuck with the guidelines. The guidelines were very helpful in another sense: they said, of all the hideous things that could come out of DNA, by far the worst idea is a human disease [in which] the disease entity is being replicated massively by *E. coli*, and the *E. coli* are escaping and possibly are going to infect people with a human disease. Not to mention the fact that if we combine human diseases, we may make a really horrible disease that's worse than ever before. Maybe you get the contagion of one bug, and the lethal nature of the other bug, and they never were together in one single bug, but now you've combined genes, and now you have this bug that does both. It's very contagious, and it's very lethal. And of course, that's the trouble with AIDS.

AIDS basically was the result that people feared when they did recombinant DNA at the beginning. They feared that you were going to come up with something that's just absolutely hideous. So, it was a strange benefit being able to synthesize the human gene instead of taking it. And the strange benefit was, come on now, if you look at this scientifically, if I've got the human insulin gene here and I've got the one that I've synthesized here, is there any possible way in which this one's safer than this one? But suddenly it's safer because the guidelines deal with human genes, and it's not a human gene, it's a synthesized gene. But the fact is, it's identical. So that was really a weird way to get around the guidelines, but [Genentech] did that. And they were launched. I mean, they just took off. Biogen in Boston was struggling with the mayor of Cambridge and getting nothing done, and Genentech charged way ahead.

Hughes: Do you think that companies such as Amgen and Abbott followed the NIH guidelines, which of course they didn't have to do because they weren't receiving federal funds, because they had a genuine concern about biohazards, or was it the politically expedient course to take?

Rathmann: It probably was politically expedient, but what was terribly politically unastute at Abbott was one little simple extra thing, and that is, "We're going to comply with the NIH guidelines, the HEW guidelines, but we're going to do it a little better." And that one thing was really punitive. The fact is, if you analyze what was the most efficient way for a company to behave, it was to understand the guidelines and adhere to them rigorously--not one iota more nor one iota less. That sounds very rigid and terribly uninspired, but that was by far the best thing. I remember the debates at Abbott, "Well, we're trying to do better than the guidelines. So, we don't want to stop right there. How will we do better? Well, we could put the whole building under positive pressure--no, we'll put the DNA rooms under negative pressure, and the other rooms under positive pressure, and that means the air will always be flowing into the rooms, so there's a much lower chance of stuff going out." Oh, it goes on and on. Some people who had little understanding of the science were rubbing their hands, because they were literally controlling the whole course of this activity within Abbott, and they had not lost control to the scientists who were potentially dangerous.

Hughes: Biosafety would have been a problem that you would have had to deal with almost immediately as soon as you became associated with Amgen. So how was that experience at Abbott translating to Amgen in how you handled this whole recombinant DNA thing?

Rathmann: The answer is that Genentech was a model of how you get the job done, and the people at Amgen, including Winston Salser, had gotten pretty well acquainted with the Genentech approaches. So there was a West Coast can-do approach that was very, very strong and very justified. They knew that you could stick with the guidelines. You didn't have to do better than the guidelines to be safe, and if you stuck with the guidelines, you could live with that. They were pretty relaxed already. The guidelines were set up, as I said, very intelligently; they told you which experiments you should shy away from. Human viruses, don't put those anywhere near a recombinant system. A whole lot of guidelines that were designed to do the safest experiments first. The safest experiments were really safe, and made it possible to do some really wonderful important things. So you didn't need to start right out with a human virus and embed it into your DNA and all that. You didn't need to do that, and we didn't do that.

Hughes: Well, let's go back, we left you stranded without an opportunity to go to Salser's lab because Salser wasn't going to be there. So talk about the offer to become CEO of Amgen and what you thought about all that.

Rathmann: Well, that came very quickly, and I can tell you the dates. It was April of 1980 that I took a leave of absence from Abbott. I took a leave to learn DNA, and they all kind of wondered what was wrong with me, but I had convinced Joy that recombinant DNA was the most important thing I had ever seen, and that we ought to try to learn about it. Joy's a biologist; she understood that this was very exciting.

J. Rathmann: Winston offered me a job, too.

Rathmann: You're right; I do remember that.

Hughes: And what was your job to be?

J. Rathmann: I don't know. [laughs]

Rathmann: Well, [Salser] wasn't so sure that he had a supporter for making a change to Amgen. So what he decided was to bribe Joy with this idea that, "Wouldn't you like to be right there in the lab with him?" It was kind of interesting.

So anyway, Winston had decided that he was going to help start this company Amgen. That was a funny story because the venture capitalists who had started Amgen had decided that they were going to put together a scientific advisory board. That was one approach to building one of these new companies: take a scientific board of real preeminent scientists, and then have that as a kind of lightning rod to attract scientists and investors and to guide your research. There are some flaws in this thinking, but it was very well accepted at the time. So, they wanted to organize a scientific advisory board, and they picked Bob Schimke at Stanford to do that. But Bob ended up with a dad who was very sick, and he had to bow out. I've known Bob now since all those years, but he did not start Amgen because he had the burden of a very, very sick father up in Seattle. So he had to factor himself out, and he proposed that they pick somebody else. He said, "Why don't you pick Winston Salser?"

[Tape 2, Side A]

Rathmann: What Winston had done, which had gotten everybody's attention out here on the West Coast, was that he had decided to build his department in a very straightforward way at UCLA. What he knew was, the more students you had, the more space you got; the more space you had, the more you could attract additional people. That spiral, which you wanted to get yourself into, could be facilitated: if you could bring some money into your department, you could hire people; you have the people, then you get the space; you get the space, you get more people, and so on.

So he concocted an idea for making money for his lab. He had noted that radioactive tracers were being packaged in very large bulk size by the people selling them, and yet a small academic lab only needed a very, very small quantity. He realized that because of the huge difference in quantity, there was an ability to do some very interesting things with pricing. Namely, if you broke down a package that cost you a hundred dollars into the small packages that were quite satisfactory for many labs, you could convert it into a thousand dollars worth of sales. So he had a money machine. And once he had that machine, he hired people with the money coming in, the difference between a hundred dollars and a thousand dollars. The people he hired were graduate students and so on, and so he now had that many more graduate students than anybody else. What his guys were doing was making money, but they were in the lab, and they needed space, and he parlayed this into a lot more space. That was what Schimke noted. Here was a guy who was clearly of that kind: he was a business guy. Strange business, but Winston would do anything to make money.

The reason I had actually met Winston was to come out here and buy his hepatitis clone from him for ten thousand dollars. Phil Whitcome had said, "If that's what you want, and you can't get it out of Abbott, let's go out there together." We got there, and I said to Winston, "I'd like to get my hands on that clone because I want to do it, and the people at Abbott are saying, 'Oh, it will take forever.'" So for ten thousand dollars I brought them back this clone so that we could make the very thing that I was hoping we could make and avoid the big biohazard stuff and everything else. Because this was absolutely safe.

Hughes: Was that the going price? Was there a going price?

Rathmann: There was no going price. In fact, I was astonished that I could even get the clone, because most of the things were shepherded and very precious and so on. But he had done the impressive thing and gotten himself a clone. When I offered him something, why, he had dollar signs for eyes, he was obviously going to go for it. He gets his ten thousand dollars, and that packs more money into his lab, more space, more students. But the sad part was that a couple years later, I had left Abbott of course, I went back to find out, "Well, how did you do with that hepatitis clone?" It was still in the refrigerator. It was one of those things. Your own ideas are much more interesting than the other guy's ideas, and if you ever want to have an idea lead to something, you'd better work on it yourself. Because if you think that automatically it's going to get picked up by somebody else, it won't be.

Hughes: But that's amazing, isn't it? It seems to be a no-brainer that a hepatitis B vaccine would have a huge market.

Rathmann: Yes, that's true, except that Abbott was not interested in the vaccine. I was only interested in the diagnostic. See, our kits had to have a positive in there that had a surface antigen. So, it was not a huge thing to do. It would be a very significant savings in the factory because you're not going to have everything thrown into a biohazard mode. I mean, biohazard mode is a real pain. I remember when we designed one of our rooms--oh my god! Because of the biohazard issue, the flooring has to be pulled up at the sides, and all the materials have to be proved to be a special grade. You were afraid that your air conditioning system, if it were just ordinary steel, would gradually rust, and then the rust would possibly hold bacteria and mean things. So everything had to be stainless steel from beginning to end.

The imposition of biosafety considerations on your space was what killed Cetus. Cetus decided to move ahead, and when Ira and I went out, they were showing us their new P3 facility, and it wasn't ready, and it wasn't ready the second time we came out. And they were doing it up right. Genentech, meanwhile, through their synthesis of course, did everything P1, and they were flying. They flew right by Cetus. Cetus was started in '71, and Genentech was started in '76. So Genentech was five years behind, and Genentech had flown by them by 1980.

Hughes: So you think that the resources put into building the P3 lab were one of the things that account for Cetus's problems?

Rathmann: Well, the whole process: not just the financial resources--the delays, and making sure that everything is okay on top of okay on top of okay. And when you've got people that can say, "No," when I'm pretty sure they could say, "Yes," it's going to lead to interminable delays. That's exactly what happened. They were not much further along after about a year after we first met them than they were at the beginning, because they were just going through this process. They eventually solved the problem, but the much better solution was to be able to do it safely and surely in a P1 facility.

In fact, all the way along, when we were doing this at Amgen, we would go into places --Phillips Petroleum was setting one up. I remember going to theirs. Man, oh man, they had rigidity in their system that you wouldn't believe. You couldn't get from one place to another without a locked door and a pass, and then certain people could get in, and some people couldn't get in. Nobody had any more hazard than anybody else. But it was treated as though in one case you had to do enormous things, and then in the Genentech case, you did very little.

Hughes: In contrast to the other stories that I've heard about the beginnings of biotech companies, Amgen was the vision of venture capitalists, who then looked around for some scientists. Is that really the way it went?

Rathmann: I think that's true, yes.

Hughes: Did any other companies start that way?

Rathmann: I don't know. These venture capitalists had been involved in the starting of Cetus and in the starting of Biogen. So to say that Biogen wasn't formed the same way would be kind of hard to argue for because Moshe Alafi was at Biogen, and several of the other

venture capitalists that we dealt with were. Bill Bowes had been involved at Cetus and so had Sam Wolstadter. The two of them were venture capitalists.

Hughes: So they knew the business as well as anybody, I guess.

Rathmann: Yes, as much experience as there was in the financing of recombinant DNA.

Hughes: But you could also argue that because they had been involved with these other biotech companies, they would say, "Well, that niche has been filled. How is another biotech company going to get off the ground?"

Rathmann: I think a version of that is what I understood, and that is, there is undoubtedly room for another biotech company. That was the statement that was made to me when there was the question of my going to Amgen.

Hughes: On what basis did people say that?

Rathmann: Just the belief that there was room for another biotech company. They figured that it was going to be very important. And, in fact, it proved to be true. [laughs] Dozens of biotech companies formed after that. There are two things. One is that there is plenty of room because there are lots of things to do. The other is that it hadn't been done quite right. The Cetus plan wasn't quite right. They became very sluggish. They got very big very fast, and they had a number of different problems. They tried to organize Cetus Immune and Cetus Palo Alto and Cetus here and Cetus there. The net effect was that they lost control of what they were trying to do. They were building up costs fast and not building up effectiveness. So, Cetus had certain unique problems.

Biogen was formed in combination with International Nickel. Whether that was good or bad, I haven't any idea, but it was different. I am sure that if you get yourself [allied] with a company too early, they might not want to spend the money or something else. I think it was the venture capital arm of International Nickel. Moshe [Alafi] said, "I'd like you to come to Biogen." He was one of the guys I met to get Amgen started, but he also had been a founder of Biogen. So he was very interested in Biogen, and he said, "George, I want you to see Biogen because maybe you'll like it better." So he had me go out to visit Boston and Biogen. He was pretty much a prime mover both there and at Amgen.

Hughes: And what did you think of Biogen?

Rathmann: Well, I thought that Wally Gilbert, who got a Nobel Prize, was an extremely attractive guy. Phil Sharp was very capable. They had put themselves in a dungeon somewhere. Boston was not an easy place to find fresh space. The business park at Amgen was much more interesting to me than going into some crummy place that wasn't clean and wasn't new at all. I was just standing there thinking, "Oh boy, I've got lots of worries if we have to start this way."

Hughes: Plus you had the legacy of how Cambridge reacted to the recombinant DNA issue.

Rathmann: Well, it was very clear you didn't want to be there unless that legacy was gone forever, and you weren't really sure.

The reason why I didn't take the job was that Biogen at that time was a Dutch Antilles company, because they had figured out there would be some tax savings in being a Dutch company. Biogen had their primary operation in Geneva, Switzerland. They had scientific advisors in Ireland and Scotland and Germany. So they were already in some trouble from the logistics standpoint. They offered me the U.S. job. But here you've got sitting over in Geneva the real job. I said, "No, thank you very much." I didn't need that idea that you were starting out a subsidiary, and there's some uncertainty here. When things are going on, and everybody's established, you could work something out. But when you're just getting started, and you start out with that kind of disadvantage, it didn't intrigue me at all, so I passed it up.

Hughes: You also have very senior scientists in charge of each of these labs spread out over the European continent and Britain. It seems to me quite a different model than for example Genentech where the early scientists were all fresh out of academic laboratories; they were starting their careers; they weren't big authority figures. It would be hard, wouldn't it, to get cohesion in a group of men who had the prestige of that group?

Rathmann: It was clear that there was a difference in Biogen relative to what I was used to at 3M. In other words, my idea of how you run a business, the 3M way: if you want to break it down into divisions, that's fine, and each division becomes a model of a company. You've got your general manager, your technical director, your marketing guy, and your manufacturing guy. Every division of 3M had those people, and every division operated as autonomously as they could. They liked the idea of autonomy as a driver of individual thinking and all the rest. So, what you weren't used to at 3M was that you set up a board of outside people. Everybody [in a 3M division] is full time, working on your program. You could be like a little company, all contained, but you're trying to act totally independently, and what you don't need, in a way, is a group of advisors coming in once every three months to tell you what to do. That was the scary part about Biogen.

In July of 1980, there was an article in *Fortune* that convinced me beyond any doubt that I wanted to be in recombinant DNA. I had planned to get an education. I had been three months in that process trying to get Winston to get me a place in the lab. But the real decision, that this is where I wanted to spend my time, was in June of 1980 when they had an article on Biogen. What they pointed out in that article is--I remember the phrase--"the scientists have their hand on our jugular." That always seemed to me to be the right way to do it. If you're going to be a science-based business, for gosh sakes recognize who's essential to that business! It's the scientists. There was always a little feeling, and at 3M it was quite clear once in a while, that just about the time when things started to move, the marketing guys would move in, and they would take over to run the business. I didn't like that very much. I just thought, have a plan that will keep the scientists committed.

On the other hand, the article also revealed that these guys, the so-called advisory board, were sort of all-powerful. They reported to the board of directors; they didn't report to the president. But when I came to Amgen, they said, "We [have] a scientific advisory board." They introduced me to four or five of the members, and [told me] that that board was going to report to the board of directors. I said, "That's very interesting, but then you're not going to have me in that company."

Hughes: [laughs]

Rathmann: They said, "What do you mean? What's wrong with that? These people are prestigious professors." I said, "If they are going to be involved in the company, they will report to the CEO, or I'm not going to be the CEO." There was a little bit of that at 3M once in a while. You would buy some technology, and in the process of convincing the guy that brought the technology to the company, he would get access to the president of the company, and by God, there were times when these guys would want to run right in to the president to tell him that the division wasn't doing it right. "You've got my technology, but it's not moving as fast as it should be because the guy running the division isn't doing it right." And he's second-guessing, and it's miserable. I knew all that, so I thought, no way am I going to have a scientific advisory board report to the board of directors and tell them what a crappy job I'm doing. No way. So I said, "No, if they report to me, that's fine. Otherwise, I'm not going to do this." They said, "Oh well, they can report to you."

But Biogen's [organization] was pretty autonomous. Not only did [the scientific advisors] run their own labs with some Biogen money, and so on, and preserve their own individual labs, which was a little scary. No, the Genentech model was much more along the industrial lines that I was used to. You set up your R&D within your company. You're going to have some advisors. They advise through the management team of the company, not telling the board what people are doing wrong. It was just much more straightforward, like what I was used to in a business environment. So Biogen was a little scary, even though as I say, I got talked into the whole idea of being in a recombinant DNA company because of that article in *Fortune*. It's a wonderful article, by the way. The intriguing picture was these seven or eight scientists in a room, talking to each other about the new things that could be discovered by recombinant DNA. It's just so exciting to imagine the extra stimulants of real geniuses from all over the place dealing with each other and kind of raising your level, kind of bootstrapping you right out to the ultimate level of understanding and insights. In fact, we did have that at Amgen. With our scientific advisory board, we had the best there were. There were many examples of how just remarkably powerful scientists can generate remarkable insights.

Hughes: The scientific advisory board had been set up before you came into the picture?

Rathmann: Yes, I had nothing to do with it. I helped a little to get Bill Rutter, but that's the only one. The others were already there, and they were set up by Winston. So Schimke in his own funny way, when he picked Winston to set up the scientific advisory board, actually picked the right guy, because he was very clever. Because what Winston did, I learned this after I got there. I went to John Carbon. I said, "John, why did you join?" He said, "Oh, everybody was lined up to get onto this scientific advisory board. So I wanted to be on it." I said, "That's really interesting." Then I said to Norm[an] Davidson, who was a prestigious guy, "Why did you join?" He said, "Oh, they had this scientific advisory board all set up, and I was one of the last to get on." Arnie Berk said, "Oh, I was given the privilege of joining this scientific advisory board." So that was Winston. Winston's telling everybody that he's got all these people nailed down, and in some cases they weren't.

Hughes: [laughs]

Rathmann: But eventually a lot of them nailed down because the other guys eventually nailed down too. We gave John Carbon an award once because he was the first member of the scientific advisory board, and he said, "I can't take this. I was the last one to come on." We said, "No, no, we've got the dates. We know exactly when you signed on. You were the first member of the scientific advisory board." [laughter] So Winston in his own way didn't hesitate to get the job done by whatever way he was going to get it done. But it was very interesting that our board was always--it was a priceless board. They were so bright and so capable and so willing to meet with the scientists. I used to make the statement, "The Biogen scientific advisory board would go off to meet in Barbados, and ours would meet with the staff in our building, trying to stimulate them into doing the right things." I thought that was very true. We had a very active but down-to-earth scientific advisory board.

Hughes: And a lot of interaction?

Rathmann: Oh, a lot of interaction. Eventually, the scientists would just as soon chuck them out of there. But for the first two years, there was no doubt that it was a very precious relationship.

Hughes: What was it in the end that convinced you to join Amgen? This by most accounts was a risky thing to do. It was not only a company whose future was a bit dubious, but the technology hadn't produced a commercial product yet.

Rathmann: The only time I had any misgivings was when I went out to Biogen at the suggestion of Moshe, and I talked to Wally Gilbert, whom I respected a lot. I had not met him before. And Phil[ip] Sharp, who was also easy to respect, and very, very prominent. And their credentials were incredible. They said, "George, we've got to tell you, you're falling into something that isn't what you think. Winston Salser doesn't tell the truth. The very thought that you think that we might invest in Amgen is an example. We have no plan, not even the least inkling, of trying to invest in your company. We would never consider it, and I'll tell you why; it's been touted around for months that Charlie Yanofsky is on your scientific board. We know Charlie; he's not on your scientific board. He doesn't intend to be. So there's so much wrong with your company. Just be sure you understand, we aren't going to be buying into your company in any way, shape, or form." That's true. They told me, "Winston has said, 'We think Biogen will make an investment in our company, and that would be so great. Boy, would that look good--one of the leading biotech companies investing in us. That would really be good.'" Yes, well, it would be good, but it had zero probability of happening. So I got shook up from that. I thought, "Gee, am I getting into the kind of people I don't know anything about and the kind of relationships and behavior that I would not want to be a part of?" So I worried. What was your question?

Hughes: Well, what really grabbed you, considering these doubts?

Rathmann: Well, that was, as I said, the only negative, because the thing that was positive was, I really did believe that recombinant DNA was going to change the way that medicine was being done. All they had to explain to me in the earliest days was that with recombinant DNA you can make a truly natural human protein. You don't have to wait for a human body to make it. You don't have to harvest it from cadavers. You make it yourself. We already know about insulin, and we know about a few others--human

growth hormone. But what we can't even imagine is all the ways in which that capability is going to change human health. So I was absolutely turned on by the fundamental science and its power.

The only thing that would scare me once in a while was if somebody would say, "It really isn't that good." Or, "It's going to have these kind of difficulties." A lot of the real worries about safety were already behind us in 1980, and the ability to do everything was seemingly pretty much in place. That was an easy call; that this [technology] was going to be important. The easy call then was, I'd like to spend six months of my life to understand something that's going to be this important. Then the changing over from being Winston's scientific collaborator, or being on sabbatical in his lab, to running the company was strictly because I had a chance to meet these scientists that were on the scientific board. They were the only people we had that were going to be with the company, but they were wonderful people. As I say, I couldn't get a hold of Marv[in] Caruthers from Colorado. They called me initially because they wanted to have some kind of recognition for him--the lifetime achievement award. Marv deserves it. He's just a wonderful human being, and he's the father of modern gene synthesis. You could not synthesize genes effectively today without using Marv's science.

Now, the way they did it at Genentech was different. It was nowhere near as good as Marv's. He came up with phosphoamidite chemistry, and it was wonderful. On top of that, he's just a first-class human being. You run into somebody like that and you say, "Well, this is wonderful." Then Lee [Leroy] Hood is the next one, and my gosh, Lee Hood is statured beyond belief, even back in 1980. And it's only gotten better since then. In fact, he wasn't even a member of the National Academy [of Sciences] in '80, but everybody knew he would be. Same with Marv; he would be. Same with John Carbon; he would be. You run into these people, and you suddenly say, "I'm going to have an opportunity to work with these people, and listen to their wisdom, and have them use their ideas in our company. I mean, this is something you don't want to pass up."

Now, Abbott asked me to start a company within Abbott, when I told them I was going to leave. That was hard to pass up. Because the chairman and president were wooing me to stay, and they said they would do whatever I wanted. They would pull the company any which way. If I wanted outside investors, that's okay. If I wanted to sell public stock, that's okay. So they made it very attractive also.

Hughes: Had Abbott ever done anything like that?

Rathmann: Well, no, they never had. They had their own recombinant group, but they had never done anything in the way of starting a company, no. They had bought companies, so they knew they could handle it, but they hadn't ever started one. That was tempting, but I suddenly realized that there were some caveats that would make it very difficult to be fully competitive. One was that they would retain 52 percent ownership of the company. So you're not going to have some of the freewheeling that Genentech had. You would be constrained.

Hughes: And you were not going to be rubbing shoulders with the top scientists in the field.

Rathmann: How are you going to get a scientific advisory board as good as Amgen's when they're not going to have that same confidence that they've got all these freedoms and all of this upside in terms of stock value and so on? It was not trivial by that time. People had gotten rich at Genentech already, and that was a potential for attracting people to your company. That's what people were weighing. I weighed it too. That is, there's a lot of risk here, but there's very likely a very fair reward. Who's to determine whether the ratio's right or not? It might be that the reward's modest and the risk is very, very high. I remember before I went to Amgen, I did see three or four other opportunities, including Biogen. E.F. Hutton wanted me to come out because they had heard that I might leave Abbott, and they were starting a company. They were interested in soliciting a CEO. There were several others. In these cases, it was clear that they were willing to talk some pretty good-sized numbers. In fact, the CEO of Hutton said to me, "Well, how much money do you think that you'd really like to make from going into this kind of thing?" I don't know what got into my head, but I said, "Well, ten to fifteen million dollars." He said, "Well, that's probably the right number. That would be doable." I didn't even believe I had said it. I mean, it's so vulgar to think that you're taking a job to get ten to fifteen million dollars. I mean, it just occurred to me, he was expecting that I would say something. If I was going to continue this discussion, I better have an answer for him, so I had that answer. I think if I had told Joy I was going to tell people I wanted to make fifteen million dollars, she would have had me committed.

Hughes: Mrs. Rathmann, what were you saying about all this risky business? The other transitions your husband had made over his career were more conservative.

Rathmann: Well, it turned out that Litton was more unknown than I ever would have known.

Hughes: What did you think of all this?

J. Rathmann: Well, it was just sort of going on. I didn't want to be left behind.

Rathmann: [laughs] Oh, you think I might have left you behind? That's not very likely.

Hughes: You weren't concerned that he was getting into a really risky business at Amgen?

J. Rathmann: I think it's funny, because I frequently used to say to myself, "Well, I can always go out and get a job." [laughs]

Hughes: I understand that you weren't particularly enamored of the idea of coming to California?

J. Rathmann: I was terrified! [laughs]

Rathmann: That was a bigger part than anything.

J. Rathmann: Although my dad's family all grew up here. I have cousins here and everything. But, it was scary, coming from the Midwest.

[Tape 2, Side B]

Rathmann: Abbott wanted to invest five million dollars into Amgen. When Abbott was going to invest five million dollars, that made this a lot more real than before that. It was Abbott, a very conservative company, and a company that we really loved, they had been very good to me, and now they were going to be involved after all. Even though I was not going to report to them, it was not their business, the fact that they made that investment, I thought it really was one of the most wonderful things that ever happened to me.

Hughes: Did that give Amgen legitimacy in terms of potential investors?

Rathmann: Well, we did it all at one time. Our legitimacy came very quickly. We had to decide how much money to raise, and I said, "I think I would like to raise more than five and maybe fifteen." The venture capitalists started explaining to me why you don't want to raise too much. You're much better off to get the rest at a higher price. I said, "Well, I understand all that." But I had a little bit of experience in St. Paul with a venture company, and I decided I could see what can happen here: the guys that have the money can hold back and hold back and then squeeze the bloody heck out of you. That's what had happened to a small group in St. Paul. I hadn't been in it, but I had been watching them. They had to go to the point where they didn't make any salary for about six months. It went on and on and on, and the squeeze was on to get more stock for less money on the part of these investor people. So I thought, no way, I'm not going to stop short. So I asked for fifteen million. They said, "Well, okay, go after any number you want. We'll go with you."

The venture capitalists, of course, had put in their trivial amounts. Each one was able to get thousands of shares for nine thousand dollars, six thousand dollars, et cetera. Six thousand dollars as a founding investor, I mean, that's really pretty cautious, but that's what they put in. But, they did go along with the idea of raising fifteen million. So when we put our offering memorandum together, to their surprise, we had the offering memorandum printed and out twenty-one days from the day when I was hired--to raise fifteen million dollars, and we raised nineteen. Now, how did we get the nineteen? That's the answer to your question. Well, when we talked Abbott into three and a half, and Tosco into three, we had six and a half out of the fifteen right there. Then when we got the idea that Abbott might be willing to put a little more, provided Tosco put some more in, then Tosco went up to three and a half, and Abbott went up to five. So we had eight and a half, almost half the amount of money we were going to raise. In fact, more than half of the fifteen we thought we might raise. That makes a difference. Yes, that sounded like it was going to make people come in for you, because they would see it there. It was very attractive to have a company like Abbott that hadn't made minority investments practically ever--they had never done anything like that--putting five million dollars in. That was a great testimonial. And we used it. But it also was very reassuring to Joy and to me; if everything else failed, we still had five million from Abbott, and we had Abbott's support. Then Tosco, which was lined up by the venture capitalists, was the oil shale company, and their three and a half, that was a big nest egg.

Hughes: You've mentioned Moshe Alafi, but there were others involved, were there not?

Rathmann: There were four of them. The first day we came out, Winston said, "I want you to come out and meet some people, because I'm taking a leave of absence myself. I'm not going to be working with you on sabbatical, because I would rather have you get involved in this company. I'm going to be starting this company." So he said, "Come on out and meet these people." We went to a place that's about six blocks from here, and that was [Franklin] "Pitch" Johnson's home. He was the head of Asset Management [Company] at the time. In his backyard, we sat there with Moshe, Bill Bowes, Sam Wolstadter, and Pitch. Those were the four venture capitalists that I met that first day. In Pitch's backyard, with these huge eucalyptus trees, and gorgeous area, gorgeous weather. Yet moving to California was one of the things we were least interested in doing. So they started working on us. It was actually the combination of those four. Pitch Johnson and Bill Bowes were both very well known even in Chicago, Moshe and Sam were not. But Moshe and Sam played a very active role in getting us. Sam was calling on the phone every day, and Moshe was suggesting the trip to Biogen, to kind of round out my interest and any other place I wanted to look at. They were all really wonderful.

Hughes: Now, Moshe, of course, had previous connections with biotech. But had the others?

Rathmann: Yes, Bill Bowes had been on the Cetus board.

Hughes: Oh, that's right.

Rathmann: I don't know about Pitch. I think he had gotten involved with some small companies, like Monoclonal Antibodies, something like that.

Hughes: Were they easy to convince that this was worth looking at?

Rathmann: Oh, I didn't have to convince them. They were already convinced; they came to convince me.

Hughes: I see.

Rathmann: You were right, Amgen was basically started by venture capitalists looking for someone to start a scientific advisory board. They tried Schimke and then they went on to Winston. Then Winston lined up a tremendously powerful scientific advisory board. The first action that board wanted to take, when I had been there here for about six months, was to get rid of Winston. I said, "I can't understand this. You guys all came on board because of Winston, and then you want to get rid of this guy. There's something funny about this." Then they said, "We think that Amgen is better than what it would be if Winston were going to be heavily involved."

Hughes: And so Winston was out?

Rathmann: Yes, he was out.

Hughes: How did he react to that?

Rathmann: Oh, terrible. A terrible experience.

Hughes: In a way Amgen was his baby, wasn't it?

Rathmann: As much as anybody's. Even more than the venture capitalists, because he had gotten all these scientists lined up. There had been a number of incidents, one of which was just a week before I was given this assignment. The one that happened just a week before was that one of our advisors had a person who was very interested in some of Winston's work, and so she went over to see Winston. Winston shared with her some of the ideas of what he was working on. She subsequently submitted a paper for publication, and Winston found out about the paper, got his hands on it, and found out that, although it acknowledged discussion with Winston, what she put in that paper hadn't been cleared by Winston. So he picked up the phone and went after the editor of the periodical and said that they must not publish this, that it was terribly wrong, it plagiarized and took stuff from Winston Salser without authority and so on. Our entire board heard the story and were so angry. First of all, this young woman was being abused in the sense that she had put her heart and soul into this, and now she was getting the run-around from some guy, playing power politics with a periodical. So our board had become very turned off by Winston. And others that had some other kinds of experiences, not all that bad, decided that Winston was not the person they wanted to be running the scientific advisory board. We had one scientific meeting, and at the end of the meeting, I said, "I want to talk to you." So I went to each one and talked to them, and they all said, "We've got to get rid of Winston." My gosh, I just got into this job. I don't want to get rid of somebody, that's a terrible idea. But I figured I had no choice, either get rid of him, or we're going to get rid of the whole board, because they had now united in their belief that he had to go. So I tried to do it right with Winston, but I didn't do it very right. He was very, very angry.

Hughes: Well, maybe there was no way to make it right?

Rathmann: To take it away from him was not easy, but Winston retained a large portion of his stock, including unvested shares.

Hughes: So who stepped into his shoes?

Rathmann: Well, I became chairman of the scientific advisory board by default, and that worked out all right, because when I finally about a year later hired the director of research, Dan Vapnek, then he became chairman of the scientific advisory board, and that was a natural transition. He coordinated the meetings of the scientific board, and what they did.

Hughes: How did you actually attract the scientists?

Rathmann: Well, there were two things we needed, and then I'll get to the scientists. One was we needed a business plan or proposal to raise the nineteen million dollars. We needed a document that was going to loosen up nineteen million bucks. Although as I say, the key thing was perhaps getting Abbott Labs and Tosco in the fold, that document was a good document, and we put it together in less than three weeks.

When I walked through the door, Winston said to me, "I want to put out our prospectus today." I said, "Wait a minute, this is as much as I've learned from my experiences in business, and that is, no, the answer to that is no. You're not putting out the prospectus today. First of all, I'm CEO, not you, and if it goes out, I have to know exactly what's in there. I don't know because you haven't ever showed it to me. So, what is your

prospectus?" He said, "The scientific board has been meeting, and I put together a summary of all their plans, and I put that in the form of a document, and that will be our prospectus." So I went to Bill Bowes, and I said, "Bill, how do we do a prospectus?" He said, "Well, you're not going to do a prospectus." I said, "I'm not? I just understood that Winston's already got one ready." He said, "It's not a prospectus, George. It's an offering memorandum. A prospectus is for a public offering. This is a private placement, and it's not a prospectus. Now, if that's what he's talking about, call it an offering memorandum. But if you're going to put that together, you better be sure that you've got a lawyer helping you do it."

"Well, who's going to do that?" "Cooley Godward has a young lawyer who is really good." (He's still one of my best friends, Alan Mendelson.) "He'll help you." "Well, okay." I went to Alan and said, "We've got to put together an offering memorandum, can you help me?" He said, "Sure, we'll just do it." He started listing things, and he said, "We'll get the help of one of the people who has already been selected to be on our board, Don Longman," who was an ex-CEO of Schering Plough." So Alan and Don and I sat down, and Alan started listing the things we had to do for getting this offering memorandum out. "If you're going to put the scientific board's deliberations in there, you better be sure that any name they refer to is approved, that you've got that person's approval. So, you better check with Lennart Olson, you better check with Vilchek, you better check with the malaria team, the Nussenzweigs."

Hughes: Oh, at NYU?

Rathmann: Yes, that's it. Alan insisted, "We've got to do all that." So he started listing these things, and Longman said, "We'll never finish." And here's this guy who has been given fifteen thousand shares of our stock because he's going to be on our board, walks away from his first assignment, and just gets up and leaves. Uh-oh, well, this is a lot of fun, isn't it?

Hughes: [laughs]

Rathmann: It was a real blow to think that now I'm on my own with Alan, but Alan was so marvelous that it was not a hard assignment.

So we started taking the scientific advisory board's stuff, and I spent about a solid week in the library converting phrases like, "What we ought to do is" into a kind of formal document, and stating how big the market potential was, and how long it would take to get to the market, and how valuable this would be. I did all that on my own, and then I came back to Alan to verify what we had to do in respect to Vilchek and the Nussenzweigs and Lennart Olson. He said, "Boy, you've got to get them to give this an okay." So I said to Winston, "I'm going to have to talk to these people to get their permission to use their names in our offering memorandum." He said, "No, no, you can't talk to them!" I said, "Winston, I got my instructions from the lawyer. I <u>have</u> to talk to them." He said, "I've taken care of all that." I said, "Well, that's good; I'll just verify." "No, you can't talk to them!" I said, "Winston, you're telling me I can't talk to them?" He said, "Yes, they don't want to work with us." I said, "Well, then I can't put in here that they're planning to work with us." "Well, they don't understand. They'll go along with it finally if we put it in there." "Winston, I just don't have a choice. We're going to have to take their names out unless I can get personal approval from them."

And we left one in, Lennart Olson--nice guy. The others were all taken out because they had no intention of working with Amgen, as you might have guessed.

Then I rephrased the whole thing, and it sounded not so folksy, with market data that I could put together. I put that together in those three weeks and sent it out. It was a necessary step. Once you raise the nineteen million, and you're out there recruiting, that's your first magnet, that you've got the money. The second is that you have a scientific advisory board, and I know I worked that one to the hilt. That is, of course, high risk. We're a venture; we may not succeed. But I'll tell you, if you impress Lee Hood, and Marv Caruthers, and Norm Davidson, and Marty Kline, and John Carbon, that you're a good guy, and you understand what you're doing, you've got a ticket anywhere in the world as far as I'm concerned, because those people are preeminent. So there's how you attracted the scientists. It helped that Genentech had created their first "scientific millionaires."

Also, you ended up with willingness on the part of that board to share the load. They would meet with the scientists when you wanted them to. We would bring the scientists here to Thousand Oaks, and then you had the local guys--Arnie Berk was a young professor at UCLA, and he wasn't overburdened with responsibility, so Arnie probably interviewed three out of four of our new candidates. Lee would interview some. The other southern California people would interview. So you would bring the scientists into town, and you would always have one scientific board member, usually two, that they could get taken to. Then you would have them meet with the group that we were starting to form of in-house people who were already hired. It was not a hard sell, and it gained momentum with each new hire.

I remember one of the first two or three scientists. He wanted to go to a real company, so he went to DuPont. It was a big blow; I thought we had him. Another guy that was Marv Caruther's recommendation, who had been really good at gene synthesis, wouldn't come; it was too scary for him. So you lose them here and there. There was one guy I offered a job to and then checked with Lee Hood who said, "He worked with the Nobel Prize winner, whom I know very well. It would be easy for me to help do this." He said, "I'll just call him up." He called him and he said, "The guy's no good." So I had to go back to this guy, who looked me up again about a month ago, well, we didn't offer him a job because Lee Hood had said, "No, don't do it." And I didn't. I wanted Lee's attention for all these people we were going to hire. I was not going to second-guess him on this guy. Interestingly, when I talked to the Nobel Prize winner, he didn't know me. He said, "Oh, great, fine, good guy." I knew Lee had a more valid picture than mine. We used the board to interview scientists and help select and actually to make suggestions of people in their labs or who had graduated, postdocs, from their labs. That was a big help.

Hughes: Were these in general young scientists?

Rathmann: Almost all of them were very, very young. There were about two or three came from companies. I don't know how we got them. A lot of people came by word of mouth. I don't think we did any particular advertising. Dennis Fenton, for example, one of our first hires, came from Pfizer. He set up a fermentation capability by the second day he was there, in a closet no less. So he was right in tune with the needs of a young biotech company. He was really great. He was really wonderful.

Hughes: Was it a consideration that the scientist came with a technology that the company needed?

Rathmann: No. Nobody came with technology to our company, as far as I can say. We would hire people on a skill basis--molecular biologists in general; cell biologists, some; immunologists, some; biochemists, some. Yet, there was nobody that was hired because they brought a unique technology to the company. We were lucky when we had a really good match. We were putting projects together as we were putting the people together. So we didn't have a project waiting that said, "I've got to have an immunologist." To get the immunologist, you said, "What's a good project to put him on?" and, "What project do we want to start?" When I think about it, it's a horrendous task. I'd be scared to death to try and do that today. I know too much. But at the time, we just charged ahead, started putting people into different jobs.

[End of session]

INTERVIEW 2: OCTOBER 14, 2003
[Tape 3, Side A]

Hughes: Dr. Rathmann, to continue with the foundation of Amgen, we talked about the scientific advisory board, but we didn't talk about the board of directors. Who was on it, and how did they function?

Rathmann: The board of directors included a number of people that had participated in the earliest thinking of forming Amgen, and that included Bill Bowes and Pitch Johnson and then in addition there was Ray Baddour, a chemical engineering professor at MIT. He had been important in figuring out that maybe Tosco, the oil shale company, would invest in Amgen. And they did. So he had a contact there that got him involved. Then of course he was clearly a very good fit; a professor in chemical engineering, and a very, very bright guy. We had a couple of others that left very soon, including Don Longman. He had been the executive vice president of Schering-Plough. I think he had been the president of the Schering Corporation before it merged to become Schering-Plough. He was supposed to be bringing us overseas contacts and other things. He stayed on the board; he ended up with fifteen thousand shares of founders' stock, but he never was involved again, and shortly after we went public, he sold every single one of his shares. That was three years later, however. He had not participated in the company. So, I think the best way to look at this is that there will always be several people who were not really committed to being on the board that won't stay.

We also had in the founding group of the company, the management, the decision that I had to reach of becoming CEO and changing jobs and everything else. I had come to California. The whole thing took about three months. In that time, they began to worry that they didn't have a CEO, so they lined up a person that they were going to call the executive vice president, Joe Rubenfeld. So he was one of the key first individuals there. He was literally retained by the company to become CEO if I didn't take it. Then when I took it, I looked at the situation, and I checked into him, and I didn't find that he was the guy that I wanted to have as my number-two man. So we had a parting of ways at that point. He was another person involved in the very early days that you wouldn't find in practically any of the literature, Don Longman and Joe Rubenfeld. Moshe Alafi stayed as an advisor but not on the board. Cooley Godward had been arranged by Bill Bowes to be our law firm. That was the deal in which we gave them a chunk of stock, and they operated free of charge for a couple of years. That was very standard at the time, so that they could get some stock. They were not taking money out of your treasury, and yet you were able to use them, a very, very fine firm. They had been attorneys for Genentech also.

Hughes: Alan Mendelson was from Cooley Godward, wasn't he?

Rathmann: Yes, he was, and he was dealt to me right away as the guy that would interface in getting the offering memorandum. He was superb. He was really superb. I pressed the founders to make sure that I had an auditing firm lined up, because they kept saying, "We can always do that." We were writing this memorandum, and we had to pick them. Bill Bowes said, "Well, it'll be Arthur Young." I said, "That's fine." He gave me a name up in San Francisco, but very shortly that guy correctly decided I should have someone down in Los Angeles. A very junior—not a very nice term—but a relatively junior partner, in fact I doubt if he was a partner at that time, Gary [Shaher?], was then

given to me to work out the details of what we should put in the offering memorandum. Arthur Young was willing to go this far, that they would be our auditors. But even to say just that, they had to audit everything we had done up until that time, which was largely shoeboxes full of checkbooks. In the audit that they did, they couldn't reconcile it by about forty thousand dollars. It turned out that two deposits had been written as checks cashed. So, it was actually a forty-thousand-dollar swing. It took him a long time to sort this out. So he worked over these shoeboxes, and came up with the idea that we were very clean and everything was fine. Then Arthur Young would sign off, and we then had our auditors. The only statement was that they would probably be our auditors or they were intending to be our auditors, or some carefully hedged statement.

Hughes: Was this just standard due diligence, or do you think that they were questioning this new firm?

Rathmann: No, I think it was purely standard due diligence. You've got to make the books balance when you start. Otherwise, you aren't sure where you are. I'm sure he was astonished at what the books were. They were literally a shoebox full of cashed checks and a lot of informal stuff. You couldn't always tell why [checks] were written. It took about two weeks, and that seems like no time at all, except that I started on October 1, and I wanted that document out by October 23. I thought I would have it out even before then. The last ten days were all hung up with Arthur Young, wondering why the books didn't look quite right. There was nothing nefarious, nothing improper. It wasn't the typical 2003 scandal about people running off with something or other. Everything was straightforward. It was just that it was rather casually done and relatively crude. But they signed off on it, and we immediately went to press and put out our offering memorandum to state that they were going to be our auditors. They wouldn't be our auditors until they were sure that things had been resolved.

Hughes: How does Bill Rutter fit into this? I know he ended up on your board—

Rathmann: The scientific advisory board.

Hughes: Yes, the scientific advisory board. I read something that made me think that at one point he had been offered the position of CEO.

Rathmann: I don't know that. It would have been a smart move. He's a very good guy.

Hughes: It must have been before you came into the picture.

Rathmann: Yes, it wasn't after I came.

Hughes: There was talk then of founding an Amgen North?

Rathmann: Yes, that was my idea. When I got there, Bill Rutter was on the scientific advisory board, along with about five or six others. We had one meeting, and I was very impressed. I would have said of the people that participated in that meeting, he was as valuable, or possibly the most valuable, of all the participants. I had heard of Bill because he had been a consultant for Abbott, and he had resigned that consultantship at one point, which was an ominous part of his history, that here he is a consultant for Abbott and much to their surprise suddenly resigns.

Hughes: Do you know why?

Rathmann: He was not satisfied that Abbott was placing proper emphasis on the science. For example, their board was pure business, and I'm sure he had some suggestions that were ignored. He decided, "This is a waste of time." Now, I don't know all that, all I know is that he resigned. Since his tie to Abbott was through a man who reported to me, I picked up a bag of embarrassment, because suddenly I'm getting a copy of this letter saying, "I no longer want to be a consultant for Abbott." A little bit of a lecture in there, but not much. But his lecture was that Abbott just wasn't placing the proper emphasis on science. He was right; they had shifted over to a much more commercial focus.

Hughes: How specifically was he valuable to you in those days?

Rathmann: Well, one of the first programs that we were trying to figure out how to do was to do something in hepatitis vaccine. There already was one emerging from the combination of—oh, it hadn't come out yet. Merck had indicated that they were going to have a hepatitis vaccine, but I don't think it had emerged yet. We thought we were in pretty good shape. We could get the clone of the hepatitis surface antigen, and we could get expression perhaps because we had a lot of good systems for expressing proteins. It did turn out to be an interesting challenge, because the most natural thing to do with the hepatitis surface antigen was to make it in *E. coli*. But you can't; it doesn't work. So, we had a backup there for yeast. On our scientific board, we had Bill Rutter, who knew how to get his hands on a clone, and we had John Carbon, who was one of the world leaders in yeast expression. So as soon as these guys got together, they got the idea, let's do hepatitis vaccine.

Hughes: Wasn't it a hepatitis B clone that you had bought from Winston Salser?

Rathmann: I bought one from Winston Salser but wouldn't be able to put that into the equation because we didn't own it exclusively. I bought some of it, but not all of it, obviously. So that would have helped getting the program started right.

But what actually happened was that about that time, we had taken very seriously changing the structure of Amgen in ways that might make Bill happier, because he was rumbling around that it wasn't quite what he wanted. In particular, he then shared his dream with me, which I thought was impractical. By this time, we had raised the nineteen million dollars, and I had laid out a plan for how to spend it over a four-year period, and felt that I was a bit locked in to what I told people when I got their money. Bill knew that nineteen million was an awful lot of money, and it was kind of too bad to waste it on a bunch of different projects over a long time period. Why don't we do something really big? Why don't we sign on to Amgen every top West Coast molecular biologist? And he knew them all, and they all liked him. He would do another sweep of the West Coast, much like Winston Salser had done to put the scientific board together, except this time these people are going to be part of the company, and they're going to be—oh, I can't even name all of them. There were at least ten, the most prominent West Coast biologists and molecular biologists. That was Bill's idea, that we'd just go get these guys. I said, "Oh, Bill, that's just so ambitious. I feel like I could lose the whole company here because the investors would say they had been stabbed in the back; their money's going to be gone in about six months, instead of four years. They had nothing to say about how we're going to move the company in a new direction. This is really

scary to me. It may be a better plan than what we've got, but to me it's a long-shot plan, and I don't think I'm going to do it." He was very disappointed.

But then I decided that I wanted Bill because I thought he was one of the best members of the board. So I said, "Well, what we can do, Bill, is we can make a bigger place for you in the company. We'll split the location, and we'll have one in San Francisco, and one down here, and you can run the San Francisco operation." That intrigued him quite a bit, and he watched us move, and I think he was impressed that it took a matter of days, and we'd had an option on leasing property up in San Francisco. We had started to talk to all of the scientists that were working with Bill Rutter at the time, and in fact had signed up about 95 percent of his lab as Amgen employees.

Hughes: So that meant Ed Penhoet and Pablo Valenzuela?

Rathmann: Valenzuela and Leslie Rawls and Graeme Bell, and there was a whole bunch that later on became Chiron.

In a way Bill was thrilled that we were moving as fast as we were, but in another sense the message to Bill Rutter was, "I can do this!" So you do a temporary lease on something, and you don't spend a lot of money until you take it over, and you do this and you do that, and all the sudden you've got a real company. So he defected. We had a lot of discussions, and the pivotal decision was that I did not want to hire every West Coast biologist and have the effort scattered all over the West Coast. Each one would probably start his own R&D program. The discipline at 3M was, you put your research in one place. If you need multidisciplines, you put them in one place. It benefits you, because you will get interactions that are all favorable. Deciding to decompartmentalize and fragment R&D is just plain wrong. It was almost immoral to me at that point because the teachings you learn earlier are more sacred than probably any other kind of teaching. That was the teaching that I was adhering to. I said, "No, we're not going to start places all over the West Coast." I didn't like the change in the strategy that would probably confuse people, and I just resisted. It didn't take long for Bill to decide he would splinter off and become another company and that would be Chiron.

Hughes: It's interesting that Chiron didn't do that either.

Rathmann: Yes, it was a grand plan that really was not viable. It could have been, it might have been, but it was such long odds. You had a very good chance of doing it the straightforward way, and why take the chance that you burn up so much money so fast that you run out of money?

Hughes: It was the early Biogen model, wasn't it?

Rathmann: If there was any model, that would have been it, yes. That was what they really did. They did fund work at each one of the places [institutions in which Biogen scientific board members were located]. Yes, I guess you could say it was the Biogen model. With the special twist at Biogen that the scientific board had great power, probably more power than the CEO, and that was something you might or you might not have imitated. Yes, it would be similar to the Biogen model.

Hughes: Did you ever have any concern about controlling Bill Rutter?

Rathmann: Controlling?

Hughes: Well, he's a very strong personality; he was accomplished; you've already said that you were impressed by his scientific expertise.

Rathmann: Well, it turned out that I didn't control him; he started Chiron.

Hughes: But you didn't worry about that part of it when you were considering him for Amgen?

Rathmann: No. Well, I assumed that he was on board and was going to do the things we had planned together. We had a lot of walks along the beach of San Francisco and kind of laid out what might happen. But there was always a velvet fist there that if he didn't get what he wanted, he was certainly prepared to defect. I saw that. I thought we'd pulled everything together, but it became apparent that I couldn't match the situation of his running the company. That was just not possible.

Now, we had one serious setback, which really decided the thing. We had decided to start to bring the north and the south together, so we would pay for having all of Bill's scientists, or at least six of the candidates, come down to Thousand Oaks and get acquainted with the Thousand Oaks people, and start to lay out how we were going to run this company. It was a terrible mistake. I just played it by ear, and I didn't do the pivotal thing at all. I should have. I arranged for the travel of these people to come to Thousand Oaks, told people in Thousand Oaks that there was a group that was being formed to be Amgen North, or a San Francisco branch, or a division or whatever. "Let's see whether we can't get some exciting synergy between these groups."

They got down there, and it was an absolute disaster because they came down there to advise the people in Thousand Oaks that the real center of everything was going to be San Francisco. Thousand Oaks scientists were there to tell them that they were happy to have a spur up there in San Francisco, but that the real center of Amgen was and would continue to be Thousand Oaks. That clash was inevitable. How I set it up was that each side was supposed to give its inputs. But there was nothing to focus on. "We want to stay together as one." No sir! The most important [to Amgen scientists] was the importance of Thousand Oaks, and what was most important to the other group was the importance of San Francisco. So even though we had started to move ahead—I leased the space on an option basis, and all these people signed up—it evaporated right then and there. There wasn't a single one of Bill's people that had any interest whatsoever in becoming the distant arm of Amgen headquarters in Thousand Oaks, and there wasn't a single soul in Thousand Oaks that was fascinated by any of the people that might locate in San Francisco and think that they were running the company. That's when Bill announced that he was going to start Chiron.

Interestingly enough, several years later, this was more than a coincidence, we had both ripened a bit by the summer of '83, and we both decided, Chiron independently from Amgen, that [we each] would go public. We made our decision and moved very fast, and we actually went public June 17, 1983, in what was a booming market up until April. In June, it was getting pretty sick, but we raised forty-three million dollars and were launched. Bill Rutter was rushing to do the same, but his timeframe turned out to be about the first or second week of July, two weeks after us. He wasn't very grateful to us for having slammed the window shut and leaving no financing worth anything. So he

ended up taking half as much money at half the price to go public. Although it was evolving during the early summer, on June 17 the market slammed. We sold our stock at eighteen dollars a share, and we were over-subscribed. A half hour later it was sixteen dollars a share. Shortly after that it was nine dollars a share. The market just collapsed. Biogen had raised a lot of money in the spring, and they too had suffered a little bit of a relapse as they were doing it. Although they were very buoyant and everything was very positive, if you analyze the detail, things were a lot more positive at the beginning of their campaign than at the end. So things had already become a little tainted, and then we just wrecked it.

The way our offering was done was so bad. The people running our offering, Smith-Barney, had had no experience in biotech yet. They didn't realize that many of the people that they were putting a lot of shares to had no intention of holding onto those shares. They were going to turn them over and make a quick profit, and that's why the sixteen-dollar price was reached in an hour and a half. Their idea was you get these shares for eighteen, and then you sell them for twenty-two, or twenty-five or more, and if the market's collapsing, you get out even quicker because you're afraid of where it might be going. That's what happened to us. We didn't hit our offering price for about two and a half years.

Hughes: Why did you choose Smith-Barney when they hadn't had experience with biotech?

Rathmann: Well, that's a very good question, and it is a very clear answer. What we were really doing at Amgen to raise money was we were following the pattern of Genentech. That was to visit companies all around the world, and see if you can't get some company interested enough to make an equity offering, a major R&D partnership, some kind of a joint venture, or something else. So, you're trying to get the leading pharmaceutical companies as an ally and finance so you don't have to use your treasury money. You finance things with what they pay you in the way of milestones and entry fees and so on. So, we were following just exactly that pattern. We were finding it increasingly difficult, in some respects thanks to Genentech because they had gone into the Japanese marketplace, promised a lot, didn't deliver much, and cost a lot of money. So we were after the fact, kind of a second wave, and that wave didn't have much steam. It was immediately apparent that a lot of the companies had become disenchanted with the Genentech equation, and that's the one we were trying to exercise. So we found out that we couldn't close on any major deal with anybody. And we were a little behind the power curve. In other words, when we thought we had an interesting new molecule—we hadn't made any yet; we hadn't purified it yet—that was the next thing they always wanted. They always wanted the thing we didn't have yet. So we would go back and forth with Ajinamoto and Takeda and Green Cross and a lot of Japanese firms, and meanwhile a couple of us were going to Europe. A couple of our team, not me, were trying to get the big companies in Europe to pay attention, and they were striking out. Then we went in the fall of '82 to Johnson and Johnson, and that turned out to be very unfortunate timing because it was September of '82, and they were all totally distracted with the Tylenol crisis, as you might remember. Tylenol was killing people because somebody put stuff in the pills. The meeting was a vast meeting with all the right presidents and everything. That was orchestrated well but was futile because they had other things on their mind. One of our last hopes was for J&J [Johnson and Johnson] to make a big investment or something. They were not interested.

So then we thought about our situation. If we didn't change anything, we would run out of money by September of '83. Some of the members of the board said, "We want to see your contingency plan. Since you're going to run out in September of '83, we want to see what you're going to do each month to stretch out those months and do some conservative cuts and all the rest." I looked at that and I thought, Jeez, I just put this team together. To start to send people home, that would just have a devastating effect on the company. It could be done—I suppose you could do anything—but I just thought that was a terrible idea.

By this time I had hired Gordon Binder as my chief financial officer. I said, "Gordon, you've got to figure out other solutions than yielding to the pressure of the board that we should have a contingency plan, because I can see where it's going." He said, "Well, let me work out the numbers." So he worked out the numbers, and in fact, he worked them to show the following: if we started cutting, and cut at a reasonable pace, we would last until December of 1983, but we would be out of people and out of money. That wasn't a happy outlook. Gordon said, "That's the way it looks." And I said, "Well, maybe we can talk the board out of the contingency plan if we had a better plan. That would be that we would have another way to raise money, like doing a public offering." Now, Genentech had had their public offering in 1980, and their stock had gone up quite a bit since that time, though not as high as it was right during the offering, when it spurted out of sight. But, the precedent of being a public company was pretty attractive. So we decided to do that; we would become a public company. Well, the board didn't get talked out of its contingency plan. They said, "You want to go be a public company? Why, we think you're smoking dope! And you better have your contingency plan anyway."

Hughes: Why did they think you were smoking dope?

Rathmann: The company didn't have anything yet. We really were struggling to try to say that we had done anything. We were very young. We started our first research with a couple of people in the spring of '81, and it was now December of '82. You really were hard pressed to say you had made any remarkable discoveries. We certainly didn't own anything. We didn't have EPO. We didn't have GCSF [later known as Epogen and Nupogen]. We had this plan for hepatitis vaccine, but by that time Merck and Chiron had gotten together, and they had one. So the best we had was a poor second. The animal program that we had hadn't gone anywhere. There wasn't any real hope for a lot of these vaccines for animals, because the farmers were putting huge pressure on the pricing, and you couldn't get what you needed. The chemical program hadn't gotten off the ground yet. We didn't have any evidence that we could make chemicals cheaper than the usual way of making chemicals. We had an early diagnostic program at Abbott, but they had total control of that. So what were we going to have?

Hughes: So the IPO was a desperation move?

Rathmann: Yes, it was. The only thing was that by the summer, we did have some things to talk about, and we played them very heavily. But as of December, they weren't too far off when the board said, "You're smoking dope." We said, "Well, come on guys, we need a little more help than that." At Fred Frank's suggestion, we looked at another realm of financing. [tape interruption] Fred Frank said, "You need money. You raised nineteen million but it's going to be gone by the summer of '83, so between now and then, all we

have to do is raise five million dollars from the original investors." So I went to our first-round investors, most of whom where on our board, and said, "Look, if you put in one for four or one for five, we'll be able to raise five million, and you'll help us attract more." Our board received this proposal in total silence.

[Tape 3, Side B]

Rathmann: So I said, "This is a proposal by Fred Frank," a really respected financial wizard. "What we need to do now is to get everybody together, and if we could get started with an investment of maybe one dollar for every four or five," and it was dead silent. I never got a no, I didn't get a yes, I didn't get a maybe. It was just that there wasn't anybody in that room that wanted more stock in 1982. There was nobody in that room that had any appetite for any further investment in this company at this stage.

Hughes: Did your heart sink?

Rathmann: I was very shocked because I thought Fred Frank's name would mean a lot. "I'm not trying to push for more investment. This is Fred Frank's suggestion." That went over like a thud. So Gordon and I had a talk after that and said, "How are we going to raise the money?" Gordon said, "I think we've got to face reality. We're not getting it out of other companies; we're not getting it out of investors. There's only one possibility; we have to go public." Well, when you do something that desperate, why, the board said we were smoking dope, because you really came to that conclusion by default. You didn't have any good reason, except that you knew that nothing else was working. That's not a very good reason.

So Gordon said, "George, I know the people at Smith-Barney. I think I could get them to agree to be our banker." So when we finally hit the board with the idea that we wanted to go public, Gordon's proposal was that the lead banker would be Smith-Barney because he had friends, and he'd gotten a kind of a partial yes out of them. Well, then Bill Bowes said, "If you get Smith-Barney, I think I could get Dean Witter and maybe Montgomery to be interested, and why don't we pursue that?" So we said, "At least we want authority to explore this. We're not going to ask the board for approval to go public—that's a long way away. But we don't want somebody thinking that we're off the wall here. We want you to at least support the idea that we're going to explore this." And they said, "Okay, you can explore it all you want, but I don't think you will get very far." So we locked onto Smith-Barney, and we found that Dean Witter and Montgomery were willing to join in on the offering. By the next board meeting, which was March, we said we would like to go ahead with three bankers.

Hughes: What turned them towards Amgen? What were you offering at that point?

Rathmann: I suspect, more than anything else, we had a lot of different pitches. We kind of figured out the idea that we were the second generation. We weren't Biogen, and we weren't Genentech. Therefore, we obviously weren't first generation, so we were second generation. As a second-generation company, we were doing things differently. One was we had a very powerful gene synthesis capability which right up to that point was precious. Within about two years, apparatus was coming up and you could do your gene synthesis in the kitchen. But right then, that was very valuable. We also had a very broad portfolio, and although that was very suspicious to some people, a lot of people

were rather impressed by the fact that if this doesn't work, you've got that, and if that doesn't work, you've got that, and so on and so forth. In many ways, we mimicked Genentech so we had animal programs, some chemical programs, diagnostic programs, and some pharmaceutical programs. So it looked as though we were unleashing second-generation technology across the board, and there were a lot of potential payoffs. The other things that we actually did talk about in the early part of 1983 were very limited. That's what the board saw: you really aren't ready; you haven't got much to talk about, except that you've spent twelve or thirteen million out of nineteen million, and so you must have done something with it. In those days, by the way, there was some logic in that. That is, that the value of what your company was some percentage of what you'd spent.

Hughes: Even though there wasn't a product?

Rathmann: Even though there wasn't a product. Even more specious was the value of a Ph.D. on your payroll. A Ph.D. was very precious. It suggested that you'd cornered some real talent. So there were actually calculations at that time of a market value per Ph.D. You would compare yourself with the other guys, and I suppose if you think about it that way, Genentech's market value was about seventy million dollars. They probably had seventy Ph.D.'s. The going rate was a million dollars per Ph.D. We had probably twenty Ph.D.'s. We didn't know what market cap we would shoot for, but it was about two hundred million when we went out. So we had a pretty good yield per Ph.D. But it was mostly because the market warmed up there for quite a while during 1983. Then it cooled off. What we offered these people was in a warming market; they're looking for a piece of property with promise. But as it starts to cool off, of course they'll turn their backs. There are no long-term friends in this business.

Hughes: Were you talking at that point about becoming eventually a fully integrated pharmaceutical company?

Rathmann: No, we didn't talk that way, and that was largely because on our board was an executive vice president of Abbott Labs, Kirk Raab. There were two phrases that were forbidden at our board meetings. I'll tell you, it all changed, but at the beginning there were two phrases. One was, "Well, Genentech does this or this." The classic pharmaceutical mentality was that Genentech was a fly-by-night. It wasn't going anywhere. So, don't give us that crap that because they're doing it, it's worth doing. Not quite that strong, but pretty close. Then the other one was, "We want to be a pharmaceutical company." Then we would get the lecture from Abbott, "You don't have any idea what being a pharmaceutical company is. You don't know how much you're going to have to spend, and how much you're going to have to do, and how many people you're going to have to add. It's a mile-wide problem you've got; you're nuts to even talk about it." So those were two things I learned not to talk about at the board meetings. But it was inhibiting, too, because if you're not going to be a Genentech, and you're not going to be a fully integrated pharmaceutical company—

Hughes: What are you!

Rathmann: A loser!

Hughes: Genentech had done more at that point than any other biotech company. Why was Abbott on your board?

Rathmann: Well, Abbott put in five million dollars.

Hughes: So they had to be on the board.

Rathmann: Yes, they wanted to be on the board, and they also wanted to watch their investment. So they had a right to be on the board, and they had an interest in being on the board. Abbott put the five million dollars in, I have to say, because of me. I had my track record at Abbott. I went after them hammer and tongs and told them great things that could be done by biotech, which were all true, but in the early days more visionary than they were reality.

Hughes: Their opinion of Genentech makes one wonder if they really thought that their five million in Amgen was going to get them very far.

Rathmann: Very good point. That attitude was pretty chilling. How long are these guys going to be my friends? Before we actually went public, we knew we had to figure out something in the way of a relationship with a company, and the closest company at that point was Abbott. We had already found that J&J had lost interest because of other things, and we never kindled that much interest. I tried to get SmithKline to make part of our early first-round investment. They wouldn't do it because they were forming their own big facility internally. The master strategy of starting Amgen had been that you get three pharmaceutical companies for about six million dollars, and then you get another six from some other rich capitalists, and you've got a nice blend. The big pharmaceutical companies keep your price up per share and so on and so on. It turned on that the candidate for the pharmaceutical companies was SmithKline, and they decided to do it themselves. Another one was DuPont, and they decided to buy New England Nuclear for a big bunch of money, like four hundred million. So they were not interested in putting cash into biotech.

I had gone through that round in the first round, and was now thinking about what company might invest. Our best candidate was J&J, and we missed. We had no really good alternative, and now when the internal board said that they were not interested in putting the money in, you go public. Then they say, "How can you possibly pull off, as the default position, going public? That's pretty ambitious." It was a pretty good spring. In other words, there was a lot of enthusiasm for IPOs in the spring. We moved as fast as we could move. But we still almost missed the window. We just caught it. It turns out that Bill Bowes' influence at Dean Witter and Montgomery helped to convince them that this was a good thing, which was a very important role.

So we had three bankers, but as we said, Smith-Barney was quite unsophisticated in the biotech industry, and they permitted a lot of stock to go to people— And these were not fly-by-night outfits; I don't know exactly who they were. It's been too long. But they were certainly tainted investors who had taken advantage—in and out early in IPOs. We were loaded with them because Smith-Barney had not discriminated that way, and they hadn't known the industry well enough to know who these tainted people were. So as I say, the only way your stock can go from an eighteen offering price to sixteen in an hour and a half is that people have their hand on their stock the second the bell rings.

Gordon wanted to be in New York because when the bell rang to sell Genentech stock, it just started going straight up. It went from thirty-five to ninety dollars a share in hours. So Gordon wanted to be there in New York when it happened to us. He was just dumbstruck when he watched the first offering go down to sixteen dollars. "Oh my god, what have I got here?" Then we had this dreadful period where it kept going down. If you're asking the other side of the coin—"Why did people want to sell our stock, and why did they sign on?"—it was a pretty frothy time there in the spring of '83. Biogen had gotten out with their IPO, and I think Cetus raised some money, and the aftermath of Genentech was still pretty favorable. They were still well above their offering price. And we worked hard at our pitch. We didn't have much to say in December when we had to convince the board that we would like the option of going public, but they didn't have to make much of a call either. We had the right to look into it further; they didn't say we would go.

By the time we went, our public offering had a lot of juicy stuff in there. Maybe it didn't pan out in every way. But we had the gene synthesis that was better than anything. We mentioned erythropoetin because we had some interest in a big pharmaceutical company, and we kind of played that up, although we didn't have the gene yet. I think we had chicken growth hormone, and we'd gotten a lot of publicity on that. We had indigo. We hadn't gotten most of that publicity yet, but we did know how to make indigo, and indigo was a hundred-million-dollar business. Of course, this variety was spicy to some people, and it helped us get interest up in the early days. The true strength of that interest was demonstrated very clearly when you suddenly find yourself in the market, and your stock goes from eighteen to nine in three months. You know that if there was that much interest, it was pretty flawed interest. Then it went down from nine to six in the next six months. Then it went down to three. That was the trend line of the Amgen stock price for the first year and half.

Hughes: Were you beginning to question your decision to become a CEO of a biotech company?

Rathmann: I didn't, but I'm trying to think of a reason why not. There were some people that made a huge difference to me. Mostly because they continued to express a lot of confidence when they could have been totally cynical. One of them was Moshe Alafi. I have a lot of respect for him. At that time, he was no longer very active. He wasn't on our board, and he was very much tied in with Biogen. But for some reason, Moshe felt that we were going to do it more right than Biogen. He expressed that to me more than once. I had a lot of respect for his judgment and the fact that he was continuing to show confidence that we were doing it right. He was right. You can't do anything overnight, and you can't be sure that the first things you do are going to be great. But somehow, people like Moshe had a sense that we were doing it right.

Hughes: He approved of the diverse program that you had set up?

Rathmann: I don't think he spent that much time with the details. I think he just felt that I was believable, and he knew we had hired a wonderful staff, very bright people. I think he was just betting on the odds that this place was going to win.

Hughes: Well, he was right.

Rathmann: He was right; we were a good bet.

Hughes: I know from talking to him that he puts a lot of credence in people and that he operates a lot by intuition. That's what he told me. So, his intuition was pretty good.

Tell me about the DNA synthesis capacity. Did that come through Caruthers?

Rathmann: Yes.

Hughes: It was a system similar to the one that Genentech had?

Rathmann: No. Genentech's came out of City of Hope, and it was much more cumbersome and less flexible than Marv's. Marv's was the latest, most useful gene synthesis. It was called phosphoamidite chemistry, and it was the substance of what Applied Biosystems is built on, the gene synthesis side. What Marv was doing right there at the beginning, and it was both helpful and not so helpful: Marv would show people a demonstration in which he would have three chemical flasks, and he would add the bases from any one of those three by hand. He had stopcocks. He would add that base to the gene sequence, and then he'd add this base, and then he'd add that base. He had three bases, and you could synthesize any sequence you wanted. He was making a point of showing people that all you need to be doing gene synthesis is three flasks and a pretty good Ph.D. chemist. It drove me crazy because we were meanwhile saying, "We have this unique capability for gene synthesis." Now in reality, there were patents that we must have thought we would get our hands on, which we did, but I'm not so sure that we assumed that we could keep anybody from doing it themselves. I think what kept people out was that all you had to do was have three flasks, know the chemistry, follow it carefully, and be in Boulder, Colorado.

Hughes: [laughs]

Rathmann: The reason for that was that the relative humidity was about 5 percent.

Hughes: Oh, so you're serious?

Rathmann: Yes. I went around trying to recruit people that Marv suggested. One of them was up here in San Francisco. He was having a devil of a time synthesizing genes. He said, "I just don't know how Marv Caruthers does it." I said, "Well, why don't you bring him out here to show you." This guy was working in a very small company, and he had no resources, and so he kept struggling to try to make the genes, and he just basically didn't make it. He was a good guy, one of Marv's earlier proteges. Marv had said, "Hire him; he's a good guy." But I didn't hire him. He didn't want to move to southern California. But also I was kind of suspicious that this guy was a turkey that couldn't make the genes after all, even though he had a deal with Marv where he could have gotten some more help, which he didn't get. He tried to do it himself. The fact was that a very important part of Marv's success was the 5 percent humidity, I'm almost absolutely certain.

Hughes: Dave Goeddel, who became the cloner with the golden hands for Genentech, came from Caruthers' lab, and yet the technique that they used for somatostatin was the City of Hope method. Now, why was that? Had Caruthers' technique not been perfected at that point?

Rathmann: Well, it certainly hadn't been. It was way behind. As I say, the first manifestation of Caruthers's methods were these three flask things, and he would set up a lab demonstration with the flasks. That was the first ability to do this with stopcocks and flasks, and how idiot-proof it was, I have no idea. What I think really is true is when you're in a dry climate, nothing in the world can beat Marv's method.

Hughes: What did that capacity allow you to do that your competitors couldn't do?

Rathmann: What it meant was that you could walk into the lab and make a gene coding thirty amino acids. We did it in a week with beta endorphin. Then what it allows you to think about doing, and Marv proposed this right away, was that when Goeddel successfully cloned gamma interferon, Marv said, "I'd like to make the gene for gamma interferon." What he thought was to kind of get around his patent, or at least to get a springboard from what he's done to getting us into the gamma interferon business. Marv was very anxious, whether he was going to get second-guessed by the board. And they did. They said they didn't think they wanted to see him do that. Marv very shrewdly said at the scientific advisory board meeting, "But I'll do it in ninety days. I'll get you the interferon gene in ninety days." Then they said, "Well, Marv has such stature, and when he says ninety days, he probably means ninety days. To pass up an experiment because it's too costly or too difficult that can be done in ninety days, come on, we aren't that arrogant, so why don't you go ahead and show us that you can do that." Now the thing was, and it was a challenge for him even, gamma interferon was probably 150 amino acids—450 bases, as compared to 90 that we had already done. So that is really very ambitious. Anything goes wrong along the way and you've got nothing.

What Marv created then was a brand new way of doing this, and you do it in chunks, and then you string all the chunks together in one shot. The ends of the chunks are all so designed as to link together with the next chunk, and in only one way. So you could actually put your ten-base chunks in a flask and have them instantly combine to form the gene you wanted because they [had ends] designed just right to couple with the next one. So he basically achieved gamma interferon in his ninety days. That we talked about a lot, that we had what we called second-generation gene synthesis. It was pretty evident we were better at it than anybody in the world.

Hughes: What happened to that gamma interferon since it had already been cloned by Genentech?

Rathmann: Right, you wondered just exactly what position you were in?

Hughes: Right.

Rathmann: And of course, you're hoping to follow your nose and find a position, but you're not yet able to chart it when you start. We now had the protein because we put the genes into a vector system and made gamma interferon. Then we started studying gamma interferon, and we compared it to the gamma interferon that you can get from Vilchek in tiny quantities. There was something funny. It didn't react the same way to certain antibodies. That was the lead that gave us the result that was the real breakthrough, which was about a year later. The Goeddel structure was wrong. And the reason it was wrong is that he didn't start the gene in the right place. He had a cysteine-tyrosine-cysteine on his molecule that was not on Vilchek's molecule. It might not have

mattered, but it mattered a lot. It mattered in two ways. It made the product very hard to work with because the cysteines were coupling, so it would conglomerate very quickly. Secondly, it was obviously not the right structure to get all the properties you wanted out of gamma interferon.

So we synthesized the gene based on the known structure, and then we got the idea that one way to have a place in the sun would be to change the molecule in some way, make substitutions in one form or another. So we would make an analog of the gamma interferon. We literally had at Amgen an analog strategy. We now, with gene synthesis, were in wonderful shape to take any protein that had ever been discovered and make a different one. If you were lucky, you found a change that might be useful. Now, there were those sort of theological arguments, "You're not going to improve on nature, because nature's had a few billion years to come up with the structure that she came up with." But others would say, "It has to be. Of the millions of structures we can make, one of them has got to be better than the natural product." So we followed a little bit of that lead in saying, "Let's cut off the carboxy terminus and the N-terminus of gamma interferon and just see what we get." The first thing we got, with careful work, was that the one with the N-terminus cut off, the cysteine-tyrosine-cysteine off, behaved the same way with some antibodies that had never been true of Goeddel's. So we knew that we had really hit on a correct gamma interferon structure, and we filed on it and thought we would probably own gamma interferon.

Hughes: Was changing the structure also with the aim of getting around the patent?

Rathmann: It was both. You had a capability, and you wanted to utilize it to the limit. The first thing you did was make the exact same thing, and that showed that your capability was very powerful. It might have been a ho-hum because you might not be able to ever do that. The idea that you can make variants on the molecule very, very easily and just pop these things in there, and tomorrow [morning] you have a variant, and by the afternoon, you have variant two, with that capability, which had never been there before, you should be able to find something interesting. Then when you find out that you've got the right molecule—and he had the wrong molecule—boy, you think you're in the driver's seat. It was fairly complicated and probably is not worth going into, but we ended up not getting anything out of it. Part of it was that Goeddel could show that in his first product, he must have had some of the correctly terminated molecules. Therefore, he made it first. He got a little guidance from us, but that's all right. The patent office issued a patent for that molecule and gave it to them.

Hughes: Well, above and beyond the intellectual property story, there's the one about the interferons themselves. You doubtless remember all the hype at that time about how these molecules were going to be cures for cancer; they were going to be useful in combating infectious disease. The press was high on interferon. So what happened with these interferon projects?

Rathmann: There was a lot more theory than there was practical success. There were people that would catalog interferon in terms of type ones and type twos. The type ones would be good for cancer, and the type twos would be good for infectious disease. A lot of this stuff was specious. It wasn't really fundamental, and it wasn't necessarily true. What happened of course was that the people at Schering-Plough and Roche, the people that had a virtual capability for alpha interferon, one or the other of them had hit on the fact

that hairy-cell leukemia could be treated with alpha interferon and cured. Hairy-cell leukemia is a very, very unusual disease, and I would venture that not a thousand people in the United States would have it. But it's a dreadful disease, and fatal, and here you have your first real demonstration that alpha interferon is the magic bullet or the magic cure. So the word interferon was the holy grail for a long time, and now you could understand why, taking one of the world's worst diseases and curing it. But from a commercial standpoint, you'd say, "Is that really interesting? You've got a few hundred people." I don't know the number, but it was very small. But, it's a clue you're able to do something really very important. From there you start looking at kidney disease, renal cancers, and some others, and you're hoping that you're going to see that same thing happen when you get the dose right.

Eventually, the infectious disease side of the equation emerged as probably more important than the cancer side, for treating hepatitis. That became a very very big application for alpha interferon. But, gamma was really more of a magic pill than we thought, more of the holy grail than either alpha or beta interferon. So in our offering memorandum, we played up gamma.

[Tape 4, Side A]

Rathmann: We placed the highest value on gamma interferon. It seemed like you finally had the perfect therapeutic that was going to be able to treat more diseases. It was grasping at straws in a way because very little was known about it. So anyway, it seemed like a worthwhile thing, and that's why we kept working with it, to the point where Marv Caruthers synthesized the whole gene. We thought we were rolling, but the ruling that Genentech was going to get the patent, many years later, after the fact, was because no one had figured out a really important application for gamma. It ended up with some value for a specific cancer and that was about it.

Hughes: Well, we wandered into the research program, which is fine, but let's backtrack a little bit to that offering prospectus, which must have contained your first ideas about the research program, did it not?

Rathmann: Well, you want to go back?

Hughes: What were you initially going to be working on?

Rathmann: That was not a prospectus. That was the offering memorandum for the nineteen million dollars.

Hughes: I used the wrong term.

Rathmann: That memorandum is available to look at. I basically wrote that. It was based on what the scientific advisors had been doing, but it was strongly pushed toward a more typical, industrial way of presenting programs.

Hughes: Would that be an SEC [Securities and Exchange Commission] document? How would I get a hold of it?

J. Rathmann: [She joins the interview] How are you guys doing?

Rathmann: I didn't know the regulations. There are a lot of hedges in there. It's not an SEC document in the usual sense. It's an offering memorandum. What I did was to try and make it as businesslike as I could. I changed all the folksy phrases that the scientific advisors had put in there, and changed it to a presentation of ten or eleven projects.

Hughes: How had you chosen those projects?

Rathmann: The information of the scientific advisors' meetings was presented to me, and I could read through things that they thought were interesting and decide which ones were the most defensible. What often happens when scientific advisors get together is that their most interesting programs are in fact not very interesting. The reason is that the most interesting programs deal with the world's largest populations of sick people, and they're almost all third-world diseases. From a business standpoint, I remember the education I got about third-world diseases at Abbott. You can dream all you want about helping a million people, but who's going to pay for the drug? You're going to try and sell it to people that don't have any money, and you're not going to sell it to them. If you want to give it away, that probably would work, but the concept of having all your eggs in the third-world basket would be a devastating mistake. You wouldn't make that mistake in presenting a program at Abbott, I'll tell you that. You would get eaten alive by, "Who's going to pay for it? Who's going to pay for it?"

So as soon as I looked at this document from the science advisors, I wasn't surprised: malaria, trypanosomiasis, leishmaniosis, and a few others were all there, in terms of really big worldwide needs. So let's solve the big problems of the world. But who's going to pay for it? It really makes you stop. Winston Salser, a very enterprising guy, who I mentioned got the scientific advisory board together, was frequently able to suggest a clever dimension. In the case of trypanosomiasis—that's the disease carried by the tse-tse fly in Africa—he decided to focus on bovine trypanosomiasis. The cattle in Africa, that they would like to raise in the East instead of the West, all died of tse-tse fly infections, trypanosomiasis infections, because you couldn't control the tse-tse fly there. So our scientific advisory board had a number of ideas, things that would maybe cause the tse-tse fly to die when it bit you, and most importantly, a vaccine for bovine trypanosomiasis so you could save the cattle population. The economics of this are going to be different. There may be no money for humans, because nobody cares that much about the humans, but if it makes a difference that you have meat production in a place where you couldn't have it otherwise, you could feed all of Africa from an area that before was totally incapable of raising cattle because of the tse-tse fly. So, that was the way it was written up in our prospectus. It was economically doable because you're going to be selling meat in the first world, not depending solely on third-world financing to pay for sick people.

Malaria we had in there, and I can't remember how much because I could not line up the Nussenzweigs by the time that I was writing the memorandum.

Hughes: Why?

Rathmann: What happened was mostly misinformation. In other words, the Nussenzweigs, a husband-and-wife team I believe, were the pioneers in trying to figure out how malaria worked, and how you might handle the vaccine at one or another stage of the parasite's life cycle. They had a lot of ideas. A very enterprising guy like Winston Salser was very

quick to point out who was the world leader in anything. He was very good at that—almost a gadfly approach and also a very vigorous pursuer. He explained to me, "In four phone calls, I can get to the leader of any field. The first three phone calls will tell me who they think is the leader. Then I go to the fourth phone call, and that's the guy. I have picked him very shrewdly from other people who are knowledgeable."

So his idea was that the Nussenzweigs were the leaders of malaria reserach; let's do recombinant DNA toward whatever structure you want to try and make that's going to be a malaria vaccine. You're going to have a long way to go, but you're at least going to have the best people working with you. So the scientists had written this up as a malaria program. Alan Mendelson saw this when I wrote it up that way. Alan's idea was to purge this prospectus of anything that you couldn't defend. So wow, right in the gunsights of Alan Mendelson was this comment about working with the Nussenzweigs. So he said very simply to me, "George, are you sure that they've agreed to this?" I said, "I don't know. I can find out." He said, "Please." That was on his list of all the things we had to do that caused Don Longman to walk out. Alan said, "Contact the Nussenzweigs." So I went to Winston and I said, "I'm going to have to contact the Nussenzweigs." He said, "No, you can't do that!" I said, "Winston, I'm finding out that I have to do it." "No, you can't do it. Trust me, it's going to be okay." Now I'm worried that it wasn't so okay. "I absolutely have to." "You don't want to talk to them." "Well, Winston, you've got to explain to me why I don't want to talk to them when I'm being instructed by attorneys to talk to them." "Well, because they probably won't say the right things." "What will they say?" "They'll say that they really don't want to work with our company. They're pure academics, and they don't want to be tainted by working with our company." "Well, Winston, how are we going to use their name if that's the way they feel?" "Just trust me, I think you can say it," sort of like they'll never know. So I said, "Winston, either I call them, or I leave it out of the prospectus." He said, "Leave it out." I think what I did was: we left malaria in, but you won't find the name Nussenzweig in there.

Hughes: Malaria is mainly a third-world disease. Didn't a malaria program have the same problems that you were describing?

Rathmann: Oh yes, there's no question. If you're going to view that problem as real, you can't put malaria in the front order of what you're going to do. But if you ask yourself, "Would there be a way to make a contribution from recombinant DNA?" There's a hundred and fifty million cases of malaria in this world. It is a major problem for U.S. Armed Forces around the world. The U.S. government might pay to solve the problem. Or you'd say that's one of the most monumental things you could do, and let's leave it to someone else to figure out how you're going to make money. But you're going to do an awful lot of good in a big hurry. So you say, "I can't resist the idea. It's a huge benefit. Therefore, someone's got to figure out how to make it pay." So you tend to do it anyway. But you change the priority. You've got much higher priority for gamma interferon that's going to treat cancer than malaria. The trypanosomiasis that was suggested by Winston, you play that one as a meat production that's worth an awful lot of money, not necessarily a third-world gift to the sick.

Hughes: Now, did all these projects that have been mentioned actually get started?

Rathmann: I didn't know how to start a company, but what seemed logical was first of all to present a very businesslike analysis almost exactly like you would at Abbott. When you go to your annual budget, you break down the dollars you want to spend, and allocate it by projects, and then you justify a project based on its return or its economic benefit. So I wanted to follow the same procedure I had known all my life at 3M and at Abbott. We had these ten projects. What happens as soon as you're authorized to spend money, you start allocating your resources to the programs that have been approved. I did the same thing at Amgen. We had decided that this is what investors might spend their money on, and they did. Now we have to decide how we're going to make this happen. So you hire your first person, and you show him the list. It's very straightforward. He said, "Oh jeez, I don't want to do that, I don't want to do that, but I'd like to really do that one." "Okay, that's your project."

In most cases, when you start, everything is a one-man project. You can't too quickly put three people on a project. That's the way you should do it, but it's not so easy. The first Ph.D. that comes through the door is going to have his own project. The thirteenth Ph.D. is going to want to have his own project. He doesn't want to be on one of the other projects or third on the list. And yet, you need more than one person in any program. So what you do is you start building. The next wave of building is going to be adding the people to help somebody on their project. So if they need a cell biologist, they'll urge you to hire that cell biologist. Now you've got two people working. The EPO project in 1982 had two people.

Hughes: Let's talk about EPO, because of its importance. Who were those two scientists, and how did Amgen choose EPO? There were so many proteins that could have been chosen.

Rathmann: The senior scientist was Taiwanese, Fu Kuen Lin, and his assoicate was a technician also with the name Lin (no relation). The concept was well worked out before I came, from the first scientific advisory board meetings. The scientific advisors had selected EPO. Now, it wasn't such a remarkable selection, because when I was at Abbott, we talked about EPO. Gene Goldwasser was down the street in Chicago, and he had come by a number of times to convince the people at Abbott that there was a big future in erythropoietin. So we talked about it a little bit at Abbott, and I knew of the molecule. When I got to Amgen, they had already done the following things: they had lined up Gene Goldwasser as what Winston called a major consultant. In other words, he wasn't broad enough to be one of the scientific advisory board members. He was very narrow. It was EPO, that was the only thing. We knew he was very important, so we'll make him a major consultant. We'll give him the same amount of stock as a scientific advisor gets, but he won't get embarrassed by the scientific advisors who might say, "He's not one of us. We're super broad-gauge. We're Lee Hood, we're Marv Caruthers, we're Arnie Berk. We're all these great people." So, we had some specialized consultants, and he was one of them.

Now, what we knew was he had purified EPO. That had been announced in '68. We didn't know how much EPO he had, but we suspected it was enough to get the peptide sequence using Lee Hood's Sequinator. The state of the science at that time was that if you had a really purified protein, and it was stable enough so you could work with it, and if you went to Lee Hood and his first prototype peptide sequencer, he could take

that purified material, and he could get the peptide sequence of the protein. He could only do it at one end for maybe ten to twenty amino acids if your sample was very pure. If it's dirty, he can't do that. As he starts cutting the end off, if it's dirty, it means you're getting mixed up right from the beginning. It's not very long before it's chaos. But if it's really good pure stuff, and Gene Goldwasser's was, then there's a good chance that if you put it into Lee's apparatus, then you will get the initial sequence. So, that was all laid out.

Hughes: Now, did anybody else have Lee's apparatus at that point?

Rathmann: No.

Hughes: So that was a real coup. That was a real feather in your hat.

Rathmann: That was a very valuable asset that we had access to. The real coup was that we had decided to sequence protein instead of capturing mRNA. Six companies went after mRNA and they all failed to get the gene. Amgen decided early that mRNA was too rare to detect and Fu Kuen Lin had the courage and the necessary talent to try to get the gene from the protein.

Hughes: Amgen was certainly by no stretch the only company working on EPO. Do you think the sequencer was one of the legs up that you had on your competitors?

Rathmann: Well, the actual first leg up was that we got early, small quantities of Gene Goldwasser's stuff. Secondly, we could sequence with Lee's Sequinator and bought one of the first two units from Applied Biosystems. If you had to try to distribute it across the world, no one would have enough to do anything with. Now, Goldwasser actually did distribute it. He set aside a certain amount of pure stuff, and would send small quantities to anybody that wanted it. So he did that, and that kind of saved our bacon from the standpoint of complying with the right way to do it. He did it the right way. He gave a small quantity to people that wanted it, and he gave us larger quantities as we were obviously doing important things.

But Lee Hood's apparatus was the second key, and that was a very important part of it. What actually happened, however, is that the straightforward theoretical solutions often don't work as well as they sound. This was another case, because the straightforward sequencing of EPO gave us about twenty-six amino acids in which there were obviously going to be some errors. Worse yet, they happened to be those amino acids that were very redundant in their gene sequence. There could have been sequences of ten or even less, and there would have been enough to pick the gene sequence that you were assuming was the one that made EPO. But what we ended up with was a combination of certain errors, and the actual proteins, the actual amino acids that we had were potentially coded by any of hundreds and hundreds of possible genes. You take alanine, for example, and there's six different codons, combinations of three bases, that will code for that molecule. You take that one, and then the next one, and the next one, and the next one. You've got hundreds of possibilities, and you're either going to try to test for all of these, or you throw up your hands and say, "I've got to find another set, we've got to find another sequence in EPO which is not so degenerate so I can narrow it down. I don't mind making fifty or sixty or eighty different probes to match up to try and pull

a gene out of a gene library, but I can't make thousands." And yet that was where we were headed once you looked at the end terminus.

What we recognized fairly early, certainly before the beginning of 1983, was that it would help a lot to get another sequence out of the protein, and the most likely way to do that was to take the protein and cut it, digest it, so it breaks. Then purify one of those sections, and then take the sequence from that end. So now you've got internal sequence of a fragment, which is really an internal sequence for EPO. Now you've got another opportunity to get maybe less degenerate gene sequences. That's what Fu Kuen Lin did. Gene actually did a tryptic digest, and we did the purification of one of the fragments, and then got the end terminus of that, and now had another piece of potential gene sequence. I think there might have been two hundred and fifty-six different genes that would fit that sequence, but we made all of those corresponding hybridization probes. If you hit on both that section and the other section, the thing you would be looking at is the EPO gene. And we were, and that's how Dr. Lin's patent worked. The whole story unfolds as both a very exciting pursuit of the theoretical ideas and a very frustrating pursuit because it never turns out to be exactly what you would expect. Dr. Lin was successful in using purified EPO and a sequencer in a way to learn something about the precious gene for EPO. But when you started learning, you had a lot of learning to do.

Hughes: At what point did you decide that the EPO project was the golden egg, so to speak? In the beginning, the way I'm hearing it, it was just one of many research projects, and maybe not even the most important of those. Is that right?

Rathmann: That's right. It's embarrassing to think that you ranked fragmenting oils with bacteria down in a well as equivalently interesting a project as EPO, when you realize the commercial potential of some of these things. Of course, if you solved the oil industry's problem, that would be a huge payoff as well. But in hindsight, you realize how very, very, very far away you were from some of those goals. And even malaria and trypanosomiasis were far away. EPO was a relatively short number of steps. If you got the purified EPO, if you got the sequence from Lee Hood, if you got some breaks—and we got a lot of breaks; EPO is a nice molecule to work with—then you had some assurance that you were going to get something beautiful, as compared to putting some bacteria down a well.

We had a mixed bag also because we had investors with different interests. I can remember those first five years at Amgen when a potential investor or a real investor would come in and say, "Boy, I'm really excited about your malaria project, not your erythropoietin." Or, "I'm really excited about chicken growth hormone." And you realize, it's not all bad if I'm attracting investors by the diversity of my portfolio. Now, there are some fundamentals that are in violation here. One is that you have to focus. When you aren't focusing, you're probably taking a real chance of dissipating a lot of money. But I kind of believe that there's real virtue in having different alternatives that are exciting. You attract more money, but you also already have a backup. When something fails, you're not dead in the water. So it wasn't inappropriate to have a multi-project strategy. But there was no doubt about it that from the beginning, EPO was the one that we had a lot of hopes for.

Hughes: There must come a point, however, when Amgen becomes a drug company? Meaning that these other projects faded away. Is that not true?

Rathmann: Well, it's up to you. You can decide you're a drug company, but you can decide also that a lot of drug companies do cosmetics and other things.

By the way, one of our top managers decided that a real payoff of interferon was going to be cosmetics. I talked to L'Oreal and some of these people. It was very interesting because I never got turned down. It was no lure to me; I just thought, I don't want to be in the cosmetics industry! Can't I do something more useful? That's a poor answer. If cosmetics were going to finance your company, you should let cosmetics finance your company. But we invited them in, and they said sure, they'd be happy to test interferon in a face cream or something else.

Hughes: What was that supposed to do?

Rathmann: You don't know. You just know that it's a magic molecule.

Hughes: Like honeybee wax or whatever it is?

Rathmann: Well, what actually happened just at that time, interferon was sweeping through Japan, and there were ads that you could see. People from Japan were telling us of interferon in cosmetics and interferon in hairsprays, with arguments that you could rejuvenate the life of the hair or the life of the face or whatever. There was bona fide interest. If you are L'Oreal, and you suddenly are the only guys that have the hair spray that contains interferon, you know that you're going to be able to play that out for a while. Now, if there's nothing there, the FDA will catch up with you and say, "Wait a minute, those claims that you are doing something for the hair, you've got to stop that." But you certainly could say, "We've got interferon in our hair sprays. We're going to put that in there tomorrow." And if anybody wants to prove that to me as something wonderful, that's up to them; we don't make these claims. I think it would be okay. But actually the Japanese did make claims. They didn't have a lot of diverse applications for interferon.

We almost bit on that one for a little while. Noel [Stebbin] was very intrigued by that. We just thought this is going to be simple.What he learned from the cosmetics people was that it's relatively easy to prove that you've got something, because you run a study of five people, and you do it several times. One of those times, three out of five say, "This is really wonderful." So, three out of five people have selected your product as the best, and that's your claim. Sometimes it seems you don't have to have anything more statistically sound than the three out of five.

J. Rathmann: I can believe it.

Rathmann: Noel was fascinated by this. He said, "You know, it turns out you can almost always prove whatever it is you want to sell to the public." Well, we almost got suckered into that one. The people from the cosmetics firms were relatively compelling. It just sounded like, "You can't miss. We're going to put it in. If it does good, that's great. If it doesn't, there still might be a benefit to putting it in if people might try it."

Hughes: If you had gone that route, do you think you could have convinced your scientists and your scientific board? I hear you that a company has got to make money, but also there's a certain element of idealism or whatever you want to call it that also is a motivator, and maybe cosmetics isn't it.

Rathmann: Yes, I think it would be hard. It's amazing: when pure scientists decide that the commercial dimension is compelling, they can be more zealous than a sound businessperson because they lose their perspective. They suddenly realize that the survival of this company depends on themselves, and they go for it.

We didn't get very far into it. The scary part was, what if there was a huge payoff in cosmetics. What if it's not all specious, but there's some real substance, that that is a bona fide application for interferon? You've got to keep examining that possibility that you're in a position to provide this material whose best application may be in a field that you don't happen to be thrilled with. But if it works, and it really does something, that commercialization could be very important to the health of the company. So you take a good look at it. I let people talk about it. I wasn't one of those persons that felt testing cosmetics was a sin! And it's still true that if there were a place for our technology in cosmetic care, we'd better take a look at it.

[Tape 4, Side B]

Hughes: At what stage did you attract Noel Stebbin and Dan Vapnek, and for what reasons?

Rathmann: The actual history behind those two people is quite different. In the case of Noel, a piece of paper came across my desk, which was his CV, so obviously he had approached a headhunter that he might want to leave Genentech if he got to the right job. The headhunter proceeded to try to interest other companies in Noel Stebbin. His credentials were very good. He had been at High Wickham with Searle, then came to Genentech in charge of biology, so he had a very nice history. I worked off of that headhunter's sheet. As a matter of fact, I don't think we ever paid a headhunter, because I picked up Noel's name from others, and I called Noel Stebbin. I said, "I'd like to talk to you." He said, "Sure, come on up to San Francisco, and I'll meet you at my yard." That's what I did. Noel had a wonderful wife, a wonderful daughter, and I was impressed by all three of them. These guys were neat people—very, very bright.

So I proceeded from there to construct the job that would attract Noel away from Genentech. I suspected because the paper had been out on the street that he wasn't all that thrilled with Genentech. That turned out to be true. He had gotten a little bit jaundiced about Genentech. Certain other people had moved up a little faster than he had, and he wasn't sure about Swanson. Ultimately, he had a great relationship with Swanson, but I think he was feeling like he was being overlooked at that point. So anyway, he accepted an invitation to Thousand Oaks. It was a mixed bag in the reactions of people down there. One guy, Larry Souza, who had very strong negative opinions about just about everything, really liked him. He <u>really</u> liked him because Larry Souza likes to see nice clean decision making. He hates equivocation. He was very, very powerful, very intelligent, a very successful, innovative scientist. He was responsible for products that created a large percentage of the Amgen profits. Larry was the fourth guy hired at Amgen.

I interviewed Noel in probably late 1981. We started the lab going in April of '81. We had about forty or fifty people by the time Noel arrived. I interviewed him, and the question was, "What shall I offer?" I think he would have liked to be the CEO.

Hughes: [laughs]

Rathmann: The job that I offered him was vice president of scientific affairs. The idea was that it would be his job to help to bring together the entire R&D organization, so he would be in charge of hiring a lot of people from science and medical and development.

Meanwhile, John Carbon had suggested that I talk to Dan Vapnek at the University of Georgia, and he was great. He was a really good molecular biologist. He was one of the first-rate ones of the world. The guy you would want to have running research. So I got Dan Vapnek. I didn't want to miss him for running my research. And then I'd got Noel, who had a lot of practical experience to help us in the commercial direction. We made it clear to Noel that he may or may not have responsibilities for research. And we made it clear to Dan that Noel may or may not have responsibilities for research. They were just to get along. That sounds a little ambiguous, which it was. It was just exactly what I had to do to have Noel convinced that he would have enough of a course to run on, and have Dan feel that he wasn't going to be overridden by this guy. They both joined with this understanding. They didn't get along famously, but they always got along. There was always a healthy skepticism on the part of Dan that Noel was a little too aggressive, a little too black and white. I'm sure that Noel was driven crazy by Dan's ambivalence on so many things. But they were both very bright.

Hughes: How did they work out the division of labor?

Rathmann: Well, Noel kept doing more of the things that were development downstream, you might say, and less and less of the real research. But he had strong ideas about how research should be done. I think he was more intrigued by a particular area of making variants of human pharmaceuticals. He was very much of the mind that you should try variants, because they are always going to be more interesting than the natural molecules. Dan was very much of the mind—I think it was almost religion to him—that you'd better leave nature alone. She's had a long time to come up with the structures for these molecules. If you can get the natural molecule, you ought to have it. If you want to try the courageous thing of making some changes, go ahead, but be careful, because you could introduce more problems than benefits very easily. Your body is tuned to the natural molecule, and we can't be sure any other molecule can do the job. History shows you that variations are usually more difficult than you thought in most systems.

The reason Noel joined, by the way, is that we gave him a heavy dose of the scientific advisory board. (We always did.) And one of those doses was Marv Caruthers. Noel suddenly saw in Marv Caruthers this idea of millions of structures that are slightly different from the natural structure. He had spent a lot of time at Genentech looking at the variants of the structure of natural alpha interferons. There were many, many natural variants, and he was extremely excited about that. If nature makes different versions of something, you ought to play with that because there might be a version that you could make that nature hasn't made yet.

One of the first things that Noel got involved with at Amgen was to use Marv Caruthers' synthesis capability to make structures that were different. The one that he worked out with one of the other scientists was what we call consensus interferon. They worked out that nature has provided us with six, ten, or twelve alpha interferons, something like that, and a beta interferon. If we take a look at all those structures, we can look for a single structure that comes closest to high homology with every one. So in other words, you might differ from one structure by five amino acids, you might vary

one structure by nine, but there is a consensus structure that's more like all the others than any other structure. So we then had to find consensus interferon. We called it that. The idea was, that nature was trying to tell us something: nature was looking for a structure; nature was looking for the structure that we came up with because that's the consensus structure. The first time that we measured the biological activity of consensus interferon, it came out twenty times as active as any [other] interferon.

Well, that's all you need. You now proved the point that nature was searching, never was successful in getting the exact structure, had a good average structure. But when we made the [consensus] structure, we had a superb molecule twenty times as active. Well, repeated measurements of specific activity are often not very validating because the next time we did it, it was ten times as active. Now, that's still clear. The next time we did it, it was between five and ten times as active. That's still pretty good. But then the real question is, what about its side effects? And those were really serious problems with alpha interferon—nausea, vomiting, myalgia, a whole bunch of problems. What if those are also being optimized in this structure? The key is, of course, going to the clinic and figuring it out. The analysts are hanging with bated breath. Joellyn Fisher just couldn't wait for us to prove that consensus interferon was many times more active, and as a result, you could cut down the dose and eliminate any side effects. That was the Holy Grail in that area. But we never could validate, in a sustained way, the big activity advantage in living organisms. While there probably was some advantage, you certainly couldn't prove that you could find a dose in which you eliminated the side effects.

Meanwhile, alpha interferon, as I told you before, had hit the jackpot with a very small jackpot, named hairy-cell leukemia, and it was not clear at all that there was a next step. So that took another couple of years before people realized that there was a very, very important area on the market.

We thought we couldn't lose. We had a molecule that embodied all the alpha interferons and had a fairly high homology to beta interferon, and if there is a good interferon, why isn't it most likely to be ours? It seemed straightforward. The ability to prove that and the amount of money you're going to have to spend, and then find out that you're still two, three, four, five years behind the lead products out there, you're going to lose your appetite for consensus interferon. That took probably five years. We must have featured consensus interferon when we came up with the structure about 1982; we must have still been talking about it in '86 or '87. I remember I expressed to the analysts that we were going to decide in 1985. We put consensus interferon in the clinic in 1985, and we were going to decide in the next year as to whether it was really doing something better than other alpha interferons. Meanwhile, alpha interferon, as I told you before, had hit the jackpot with a very small jackpot, namely hairy-cell leukemia, and it was not clear at all that there was a next step. So that took another couple of years before people realized that there was a very, very important area on the market.

Hughes: Stebbin came to Amgen in about 1981?

Rathmann: Late '81, I would say.

Hughes: I'm guessing that he came around 1980 to Genentech. I don't think he'd been there long.

Rathmann: I think about two years.

Hughes: Well, the reason that I'm interested in the timing is that the rationale for bringing in Stebbin that I've heard was that there was an increasing realization that it wasn't enough to just clone a gene, that you had to know something about the biology. The realization arose from various unsuccessful research projects, such as thymosin at Genentech, where they didn't get very far in producing a drug because they didn't know enough about the biology.

Rathmann: So, that's your explanation of why he was attractive to Genentech?

Hughes: Yes, right, because he represented biology.

Rathmann: Yes, he was the director of biology.

Hughes: Was it a given for Amgen at that point, that it wasn't enough to clone a gene? That there had to be biological understanding? Was that what Stebbin represented to you?

Rathmann: Well, he didn't represent that to me. The part that was attractive to me in Stebbin really relates to what we had as the cross section of people at Amgen. At Amgen, most of our people were right out of academic appointments. There was about 10 percent that were different. But most of them had been only as Ph.D.s and postdocs. What Stebbin brought as far as I was concerned was a lot more experience on the practical side—of scale-up, and going into the clinic, and development studies. Dan Vapnek had no experience in those areas. He was a pure academic at the University of Georgia, but a wonderful molecular biologist. So it was pretty obvious that he could accept the idea that Noel brought something that we had no experience in. They didn't get along all that well, because about every six months or so, Noel would come in and say, "You kind of told me when I started that we were going to have to do a little dancing. Every once in a while, you get tired of dancing." The dance being, how you worked with Dan, and how you decided what your goal is. I would clarify the dance for him a little bit, give him some reassurance that he had a spot, and he really did. He was much more downstream from Dan. Dan wasn't worried at all about it. Now, Dan was not stupid. No, Dan was a very, very bright guy. If you told Dan he had to develop commercial processes, he developed them, there's no doubt about it. But his preference was a very basic science approach. But they got along well enough. They certainly performed. What we got out of the combination was wonderful results. There is no doubt about it.

Hughes: I saw a reference to Dan Vapnek and his runaway plasmids. What was that about?

Rathmann: Well, it was the source of an even more important breakthrough, which was walkaway plasmids.

Hughes: Walkaway?

Rathmann: Yes, that was the one guy's version of what they came up with at Amgen. Runaway plasmids were simply a refinement of what was going on in almost every molecular biologist's lab. But a very important refinement. The average molecular biologist's lab had realized that if you want to put corn genes into a bacterial cell, the best way to do that, instead of trying to just put DNA in there and have it floating around, or put DNA

in and integrate it into the chromosome, there was something else to these bacterial cells that were extremely attractive. This became a fundamental part of [Stanley N.] Cohen and [Herbert W.] Boyer's technology, and everybody else's. It's remarkable, but they all recognized it very early, and that is that within these *E. coli*, there were little rings of DNA, and they were called plasmids. If you wanted to do something quick and easy, it was easier to break open a plasmid and insert the DNA that you wanted and put it back into the cell, than anything else. It was a very convenient vehicle for transporting genes into the cell. So, the plasmid was the target for most molecular biological splicing.

Now, what was clearly a potential benefit, which I would have never thought of, but the molecular biologists did right away, was what if you had a way of causing the plasmid to reproduce itself? Now you could be producing a whale of a lot more of the thing you wanted. You could almost overwhelm the cell because this one little plasmid, that now contains your gene of choice, is now multiplying itself and becoming a runaway plasmid. Now, the nice thing about that would be that you have many copies of your gene and it's going to make more product, and that's going to be nice. The disadvantage, however, is that you never know where you are, so you don't have much control of this process. You might have ten plasmids or you might have a thousand. That means that your controls of your process are in question because the process is in question. You don't know what you're really dealing with at any one time. So if you had a walkaway plasmid, that would mean in their minds that you would contain a number of replications. It would be significant, but you would get less and less rapid multiplication as you reach certain levels.

The way I picture it, and I sure don't know if this is right, it's like, I'm going to make fifty plasmids, and I'm not going to make any more, and I'm not going to have this thing run away from me. But I still have made a lot of them, so that's why we called it a walkaway—a walkaway system. It was a discovery at Amgen, and named there. I don't know if anybody else ever used walkaways, but they were important to us. They made a very nice control process with very high yields.

Hughes: Cohen, Boyer, remember there was a replication site on that plasmid that they used, right? I mean, they were cloning as well as splicing DNA, right?

Rathmann: Yes.

Hughes: Was that a runaway plasmid?

Rathmann: You're cloning for sure, and you're going to replicate for sure, but the question is the relative replication rate of the DNA in there, and the plasmid. Every time the cell divides, you made another copy of the DNA, and you probably made another copy of the plasmid. But those could be independent events. You could be making multiple copies of the plasmid, without making multiple copies of DNA.

Hughes: I see.

Rathmann: That's what the runaway is. At the University of Georgia, they reported some of the first runaway plasmids. Of course, Amgen people could have read it anywhere. But it was helpful to have Mr. Guru [Dan Vapnek] in that field. That was very useful.

Hughes: Did Amgen in these early days ever consider monoclonal-based products?

Rathmann: Oh, yes. In the very early days, as you might simplify the field, there were two kinds of biotech companies. There were the recombinant DNA, which was really quite a broad spectrum to go about doing it, and your targets were pharmaceuticals and therapeutics, or diagnostics, or animals or something. But there were also monoclonal antibodies. There were three players, one of which was Monoclonal Antibodies. The other two were very formidable, Hybritech and Centocor. The business strategy of those companies was based on the discovery in 1975 of monoclonal antibodies. They would make monoclonal antibodies. They had a business strategy in all cases that you would start out by making some kind of diagnostics, and then you would eventually use human monoclonals to administer to people the capability to have the antibody fasten onto a tumor site and possibly kill it if it carried a dose of toxin or radiation. So you had these two kinds of companies, and Centocor and Hybritech were the leaders. Hybritech disappeared and became part of Lilly. So, Centocor had its own place in the sun.

Hughes: People started with diagnostics because they were easier to produce than therapeutics?

Rathmann: Yes, the idea was that you wouldn't have to go through twelve years of FDA, and you could be developing commercial products much more quickly. But there was a limitation. Although Abbott had proved a few years before that the limitation of diagnostics wasn't so bad, for those people that were trying to attract heavy financing for a biotech company, you had to offer more reward than a potential three-million-dollar diagnostics business here or there.

Hughes: There was Genetic Systems too.

Rathmann: Genetic Systems was the other one, up in Seattle, and they sold out to Bristol-Myers. They were the one-two punch. Hybritech sold out to Eli Lilly at a huge number, and the guy running Genetic Systems, who I know very well because he was the CEO of Icos, was enterprising enough to say, "Boy, this is the time to get out of this business and get somebody to buy in that's big and rich." So he sold out to Bristol-Myers.

Hughes: That was Robert Nowinski?

Rathmann: Yes. Two of the companies disappeared from the scene almost within six months. And for good reason, because the first sale was such a big price that people couldn't believe it.

Hughes: Also didn't it prove more difficult than expected to develop therapeutics on the basis of monoclonals?

Rathmann: Well, that may have been in the minds of the people that sold out, and they might have said, "I don't think it's going to be such a good trip." But it wasn't obvious to the rest of us that there were any big disappointments there. It's always going to take a long time to develop a therapeutic.

Hughes: What did Amgen do with monoclonals?

Rathmann: Well, we had the capability for several reasons. One was that the ability to make antibodies would help elucidate the kinds of structures that you had. Then we signed on with Abbott in 1983. A key event was to settle a dispute that we had with Abbott. The dispute with Abbott was that when Abbott made their original investment, they had a one-page letter agreement; these were very, very standard at the time. When a corporation made an investment in your company, you gave them something. What you told the rest of the world was that you gave them very little. What you told them was that they had everything. And the letter would determine what they had. What Amgen agreed to with Abbott was that Abbott would have the right of first review on any program that we had.

Hughes: Oh, really! That was a big deal.

Rathmann: Well, careful, the words are stated very carefully: "first review." Now, if you're contracted correctly, there will be limitations on what you can review, how often you can review, what rights you really have. There were terms in there that would suggest that you had 180 days for that review, and that was it. If Abbott and Amgen had not reached agreement by the end of the 180 days, Amgen could take the item or product or project or whatever it was to another company, with impunity. We had no permanent obligations to Abbott. If we didn't want to make a deal, we let 180 days go by, and then we could do what we pleased. That's why first review is really quite limited, and people didn't get too shaken up over it.

On the other hand, I still was afraid about which stuff would be reviewed. What if they decided that they weren't going to review it yet; they would take their 180-day period later? That was a little scary. So I put into the letter of agreement with Abbott "at our initiation." Because if we had the need for some possible outside financing or other purposes, we could initiate the 180-day period and bring it to their attention. But what was sure that we couldn't do was just take something out of our bag and sell it off to somebody without showing it to Abbott. But that's all they had. When I'm acting like it's *de minimus*, in many ways it is.

At the same time, it was the basis by which Abbott started to take advantage of us. That was, "No, we don't want to review it yet." And I said, "Wait a minute. We've got the right to offer it to you, and then you have 180 days." "Well, let's talk about that." After about ninety days, we would say, "The ninety days have already gone by." They said, "We haven't started yet." They became more and more aggressive that what they really wanted was the ability to make a deal on any one of our projects whenever they wanted to, and that was not what we had in mind. So a couple of things happened. One of them was, I went to Jim Vincent, who cut the original Abbott diagnostic deal with us. He was now at Allied, and I got them interested in working with Amgen. His attorney was in disagreement, and then they got all worried over what Abbott might do to us. I got pretty mad because I thought that we were pretty well protected, and we were. I felt that I had to go back to Abbott and renegotiate something. What I elected to do was to get Abbott interested in a diagnostic program with Amgen. I wanted a big one, and I knew that I was valuable property in diagnostics. So I went to them and suggested a four- or five-million-dollar-a-year program, for five years—a nineteen-million-dollar program. They decided to buy that. That also buried the hatchet with respect to this agreement that they were starting to misconstrue. I heard later that Bob Swanson went nuts. He said, "Nineteen million dollars. What does Amgen have that Genentech doesn't have?"

[Tape 5, Side A]

Rathmann: We knew a lot more about diagnostics than Genentech. We were way ahead of them.

Abbott sued us, because they said that we weren't behaving according to the contract. Then we threatened to sue them. The number I picked was one hundred and fifty million dollars. It was an antitrust suit, because I felt that they were preventing us from working with others, and they were a dominant force in the diagnostics field by that time, so that's against the law. So I threatened them with a big suit. They threatened back, and then we said, "Hey, this is dumb. Why doesn't the CEO come out and see me, and we'll see if we can't talk." Bob Shellitorn, the CEO, elected to come. We met in Palm Springs. In one day, in his own handwritten scrawl, we had a nineteen million dollar deal with Abbott.

Hughes: Wow.

Rathmann: And that, of course, I felt was absolutely essential. We couldn't go into a public offering in the summer of '83 with Abbott and Amgen suing each other. So we had to settle it, and that was a very favorable way to settle it, because we now had nineteen million dollars coming in, and we had a nice relationship on diagnostics. That became an important part of our research. It was also a neat thing for me because we had started this lab at Boulder under Marv Caruthers, because he wanted to have his own private thing, and now I had something to put into Boulder that would pay the bills, the Abbott relationship.

Hughes: Was it considered a division of Amgen?

Rathmann: Well, we called it a subsidiary, Amgen Boulder.

Hughes: What was it to do?

Rathmann: Well, it was to please Marv Caruthers in a way that it was also satisfactory with me. This was very common in the early days of biotech. You would have somebody like Cohen who wanted his own branch of Cetus, Cetus Immune, and then you had Agracetus, and then you had this and that. Those things turned out to be horrible mistakes, primarily for one reason. In their desire to elevate the importance of the subsidiaries, they set them up with their own stock. So if you were in Cetus Immune, you would get Cetus Immune stock, not Cetus stock. That was really neat, because now you had more control over stock value. That wasn't so neat when nobody knew how to make that stock negotiable. What do you sell it for, and how do you make sure that someone's getting something out of it? If they get no value, they might as well stay at home. If they get too much value, suddenly the guys in the subsidiary are making tons of money, and the home-base guys are going to have a fit.

So what I did when setting up Amgen Boulder—I had seen all that happen—I resisted having a stock for Amgen Boulder, but that those people would get Amgen shares. And they were literally right smack in the middle of our payscale, in the middle of our options scale. It didn't quite work out that way because our personnel people kept harping on the fact that Boulder had a lower cost base than Los Angeles, therefore we should maintain some kind of salary differential. I fought that tooth and nail. I just said,

"Hey, we're one company. We can't punish these people for being in a lower cost base." They said, "They were not being punished, they're able to get by on a lower cost of living, so they should be able to get by with less money." No, let's forget that. So I fought it quite a bit, and we ended up with the same base scale in both places. That had serious consequences. That was, you couldn't pull anybody out of Boulder and put them in Los Angeles. So we had no reason to hope that we could integrate these people back and forth. You couldn't get anybody to move out of Boulder; they were getting the same pay, and they had much lower costs, and they were in the mountains. So we never did get proper integration, but we had a very effective organization.

Hughes: How long did it last?

Rathmann: I guess it exists today as a subsidiary. It's all Amgen.

Hughes: What was Caruthers initially working on?

Rathmann: The first thing that he wanted to work on was synthesized genes. He synthesized gamma interferon genes.

There were quite a few now that I think about it. Most of them weren't that important eventually. But one of the other things he pointed out to me was that with the ability to make gene sequences, short ones like ten and twelve bases, you could be a vendor of gene sequences. If people wanted fifteen bases in a row, you would make it for them, and send it to them. The price tag for this, if you counted it out on a pound basis, was about a billion dollars a pound. So you're selling your stuff at a billion dollars a pound, but you're selling micrograms at a time. As a matter of fact, it becomes a relatively complicated business for what might be ten or fifteen thousand dollars a year. So you know on the one hand it is going to be profitable because you know you're selling something at an enormous cost per gram or per pound. On the other hand, you're doing a lot of Mickey Mouse bookkeeping and everything else for what's a half a million dollar business, so it's pretty small. The first thing Marv saw was that you could be a business selling hybridization probes and short gene sequences.

Hughes: Fairly soon, didn't gene synthesizers come in?

Rathmann: Yes, it's hard for me to picture the exact date. It was certainly after '82, and it was probably before the end of '83.

Hughes: That was going to kill that business, wasn't it?

Rathmann: Yes, that would kill that business. We never got into it, so it didn't really kill our business, because we recognized the impracticality of the number of potential buyers and the total dollar figure. The price per pound always stayed very attractive, but overall it wasn't an attractive business.

Hughes: I know from reading the Chemical Heritage Foundation oral history that 3M had a policy of giving scientists 15 percent time to work on their own research projects. I wondered if you had anything similar at Amgen?

Rathmann: Well, we probably did, but it wasn't given the visibility of the 3M system. 3M really advertised that scientists had 15 percent of their time. Although when I was hired by 3M, it wasn't a factor in my thinking because I was in love with the project I had. I didn't need 15 percent of my time for something else. I liked what I was going to do, so maybe that's why it didn't affect me. I certainly used it myself when I was recruiting for 3M.

Hughes: I presume that you coined the term "exploratory research."

Rathmann: At 3M they called it exploratory research, project 99. In every division there would be exploratory research, and you could charge it. Even better than that was that you didn't have to identify it and charge it to anything. You just did it. There was certainly a lot of that at 3M. The reasoning being that no matter how acceptable it is, if some boss looks at a piece of paper that says, "We spent $95,000 last year on exploratory research," the next thing he's going to say is, "What did I get for it?" All you have to do about exploratory research is keep asking, "What am I getting from it," and it ceases to exist. People can't tell you what they're going to do with it when they don't know what it is yet, if it's truly exploratory.

But the idea with 3M was pretty well respected, and it's pretty solid. That was, you ought to have a chance to sell your idea to management by having a certain amount of time and money you can put in to test some idea. Then you have enough information that you can sell it. At its best, that's how the system worked.

Hughes: But what about at Amgen?

Rathmann: I think we had the practice without the power. We had plenty of these. I remember Joan Egrie was in the EPO program, saying, "I think there's something really funny about the way antibodies are reacting to our molecules." You knew that she was investigating on her own what was interesting there. We didn't have a lot of problems with that. One of the ways you accomplished the 3M result is that you aren't super quantitative in accounting for people's time and place. You don't try to run it to the nearest half hour, and therefore there is enough slop in the system that someone can easily put in six hours a week, for a few weeks at least, without running into a problem, and somebody saying, "Oh, look at your output. You're not spending enough time on these other things. You must be spending some time on something else." You aren't that quantitative. I think it's very important. I think the 3M system had a lot of value, because what it does encourage is initiative, and that's one of the keys to really successful R&D, particularly in the front years. Development can't be run this way, because you've got time dates, and all the rest you've got to adhere to.

Hughes: Well, it seems to me a system that would be particularly apt in early biotechnology where so many scientists came from academia.

Rathmann: What turns out to be a driver of some level of bureaucracy is the interdependence of the scientists that are on any kind of a program like the kind we put together for Amgen. In other words, those ten projects had real objectives, and even though you're running a project, you're dependent upon several other groups to meet your goals. For example, you might be depending upon a fermentation group to make fifty micrograms of your material. You might be dependent upon some protein characterization group to

determine the exact structure of the protein which is made. Scientists are very much a part of the right direction here. What you can't afford is to have someone promise you a certain reagent or a certain result April 1, and then find out you're still waiting for it in September. You start to go stark raving mad because your whole timetable is hinged on somebody producing something for you. So the interlocking of the various types of groups and the types of things you need tend to cause you to say finally, "Hey, I'd like to see a little more planning around here. I've waited for six weeks for the monoclonal antibody people to give me a monoclonal antibody, and I'm tired of this. I needed it six weeks ago." And so what you gradually put together in the planning is a series of short interval scheduling which ties everybody together with goals that are compatible in the system. If the guy in the monoclonal antibodies place says, "Hey look, I'm swamped. It's going to be at least six weeks before you get it," you have some choices. You might go to an outside supplier, or you might suggest ways in which you could put more pressure on this guy to get it done. But, you get pretty bruised if you are inclined to have a totally flexible nondemanding timetable, because some people are injured every week. You catch on that some degree of planning is very, very helpful.

The same thing is true, by the way, with compensation programs. Everybody wants to be treated as individuals in compensation, but I found it to be very easy and very acceptable to have a salary policy that was right out of the booklet of Abbott Labs. In effect, everybody wants to be treated like an individual, but not too much. They like to think that there's a system there. They'd like to think that they have a reasonable chance of going from here to here to here, and if you don't know where here to here to here is, it gets to be very perplexing. So it turns out yes, you can put it in place right off the bat. I made a salary schedule the first month of Amgen that says you're going to be in this group or that group or this group. You're going to have this much upside in that group before you must get promoted to get increases, things like that. The whole thing was all worked out in great detail, and it actually saved a lot of grief. So some bureaucracy is very efficient.

Hughes: And the reward system was built into that plan, too?

Rathmann: Oh, yes.

Hughes: Would you tell the story about the P word?

Rathmann: [laughs] That's an Icos story. If Amgen was largely academic, Icos was that squared. At Amgen, we actually had some commercial people, like Noel, and some more commercially sophisticated people. But Icos formed right out of academia, and why was that? Because the concept that [Robert] Nowinski had was, as he said, "We're going to hit the ground running. And the way we're going to hit the ground running is that we are going to pre-recruit a staff and promise them a job six, eight, nine months later. If they show up for that job, they get to keep their founders' stock. If they don't show up, we get to buy it back for what they paid for it, a penny a share. So there's going to be a big economic incentive for them to show up to work when we open our laboratory doors. And the way we're going to pre-recruit is we will promise people a job." And the date that they picked was in September of 1990. "And you'll have a job. And we want you, and we want you," and largely we got who we wanted. They all showed up September 1990. Icos got a buy-back price at the price that you paid if you don't show up in September.

Now, if you're going to do that, it automatically dictates that almost your entire staff is academic, particularly if you pick September. That's a great time to be able to rely on people showing up for a new job. If necessary, they've had their summer vacation if they wanted it, or they've quit their academic appointment. So, if you're almost all pure academic, it's pretty straightforward to hire, as we did, sixty-five people to report to work on September 26th, and that's exactly what happened. As a result, however, you've got a very academic staff—really academic. Very smart people, very good people, pure academics.

Once in a while, you ended up with somebody who really was so ill-suited for a company that you wouldn't imagine that we would pick them out in the first place, except they had no idea what they were getting into. One of these was Mary, and Mary was the one who said, after a session in which we had an all-personnel meeting in which we said it was very important to have everybody in sync with what we were doing. And it certainly turned out to be true here. She went to the all-personnel meeting, and she came out, and she was extremely stressed. She just never expected something like this, and there it was, glaring, the P word. When I heard about it, I immediately played the straight guy, exactly like her boss had. "The P word? What word is that?" And then she said, "Well, you know the P word." "Profit?" "No, not profit—product!" Oh, so it's a sin to be talking about products. It's bad enough if somebody objects to profits, that's pretty tough, but it's pretty common. Objecting to products—what the heck are they there for? Well, they are there for science. Their understanding was that this was going to be a place of great science, and some of the academics were recruited with that in mind. In other words, sometimes recruiters are susceptible to telling whatever they have to tell somebody in order to get them. For some of these scientists, in order to get them, someone promised them the moon as far as freedom to do basic science. That's what Mary thought. She had understood that we were not interested in profits and products; we were interested in good basic science. She left about six months later. We had quite a few like that. We had some at Icos that really couldn't have done anything practical.

But that wasn't as true at Amgen, as far as I remember. We did hire some business-oriented people right from the beginning. Dennis Fenton, who is still there, came straight from Pfizer. And Noel had had experience with High Wickham and with Genentech. Searle was certainly a big company, and Genentech was a biotech company, so they were kind of free-wheeling compared to the rigidity of General Motors. We had at Amgen more people who had some business background, but not many of them.

Hughes: And then you yourself, of course.

Rathmann: And I had some background.

Hughes: In contrast to Chiron, for example, where all the founders were academics.

Rathmann: That's right. The same way, with Ingene, which was formed shortly after Amgen was formed. They had three professors from UCLA, one of whom is Gary Wilcox, who is now up at Icos, and has been for many years. But they had these three professors, and they just splintered off from UCLA and started this company Ingene. They were straight academics, and initially they treated Ingene as an academic activity. They would go in Monday morning and review the science just the same way they did their labs at UCLA.

That went on for years, and eventually it became a fairly successful company. Then it was sold out to Xoma. But at that point it still had no commercial results.

Hughes: We haven't talked directly about culture. What was it like, and did you try to nurture certain things in Amgen culture?

Rathmann: Well, an interesting insight: I arranged for a meeting with the 3M people. I didn't go out that time; Dan Vapnek and several others went. When they came back, they had a remarkable comment, "Man, I know where we got what [culture] we got." As you hear the story of 3M, there's a lot of that culture that was baked into Amgen. At least that was their observation, and I knew it was true. I couldn't deny that I thought 3M was a wonderful place, and I obviously would like to do it [at Amgen] in many ways the way they did it.

One of the first messages, of course, is that culture is very, very important. The way that you set up the organization will determine not only the outlook of the culture but the integrity of the organization. Everything else can hinge on what kind of guidance goes into the first relationships that you have with the people you hire. There was no question that all twenty years of 3M put indelible marks on me that you want to have the highest integrity at all times. You want to give a lot of respect for individuality and initiative. You want to reward initiative whenever you can. You want to be very careful about people who are risk-averse, that they will never do anything. At 3M it was considered a virtue to go out and stick your neck out, even to the point of being a huckster for something. To say, "I believe in this. I want to do it." That was considered to be something you could do with impunity because they encouraged it so much that you almost didn't have to stick your neck out because agressiveness was an acceptable behavior. So, when you have a chance to start a company, and you see some of these things that seem to correlate very well with success and with the best attitude you can get out of people, quite naturally you put that in place. I think Dan's observation is correct. I really had attempted to transport the 3M philosophy to Amgen. It was surprising. I did the same thing to some degree at Abbott. But Abbott was a very different company. Abbott was much more rigid than 3M. It might have been partly because of the great risks of health care compared to making scotch tape.

Hughes: Well, what would you like to say that hasn't been said?

Rathmann: I like to think about what really made the whole thing very exciting, and how you make the story of it exciting. I think it's partly the transformation that occurs if you're doing effective things. For example, there was a fairly significant time on the EPO program. Joan Egrie ran it, and her comment was, "Is there life after EPO?" I thought that was very revealing because what it really meant was, this is a very dark tunnel, and it's gone on for a long time. We assumed that there was a light at the end of the tunnel, and we hoped we had found a way of going at it. But what you really are saying is, "Can we hang in there long enough?" It's there; undoubtedly something wonderful can happen, but, man, this is tough times.

At that stage, we had a lot of different efforts to try to figure out where the EPO gene could be found and produced to make EPO. We were frustrated from so many different angles. The ultimate frustration, we were able to correct. The ultimate frustration was that the amount of material we were getting from Gene Goldwasser was just plain not

enough to do anything useful in trying to understand the structure of EPO better so that we could find the gene. He had very good reason to hold back, because he didn't know—we might just waste the stuff. It was the only stuff he had for his remaining twenty-year career, and he sure as heck didn't want to dissipate the resource that he had, to have us blow it away. The darkest hour of EPO was when I sent the group out to Goldwasser. I said, "You convince him that you're going to work with the thing effectively, and you're going to get somewhere." The first thing they did was establish, by kind of perusing his place, that he had a lot of the material, and he was storing it very fastidiously. The next day he was convinced he had to loosen up and give some EPO to us. The next thing that happened, within a month, we had the gene.

Hughes: Oh, really, that quickly?

Rathmann: Right. They knew that the quantity of the material could make a lot of difference. But if you keep below that level, you might go on forever. And if you're waiting to get the breakthrough before you release your material, that's a self-defeating strategy because it means you never get more material, and you never get the breakthrough. So it really led directly to the tryptic digest of those specimens. The information from other parts of the molecule as to what the gene sequence was likely to be was exactly what we needed to find the gene.

There were a lot of dedicated people in that program. I think there were about twenty by the end of the year, but there were six or eight at this point, and it was pretty grim. They were working hard, and it looked like there was no real end. Plus the fact that I went out to see Wally Gilbert to see whether they already had it at Biogen. I thought, maybe the easy path here is to give up. It was tempting. I might have breathed a huge sigh of relief if I got the statement from Wally Gilbert that they already had EPO. I would react, "This is the greatest; we don't have to work on EPO." Instead, I learned they did not have the gene but thought they were close.

Inventing with recombinant DNA is different from what you encounter in most research laboratories, because what you are really inventing is something that nature has already done. You know there's an EPO gene. You know it's extremely important. That's all there to give you the confidence with this black hole that you're mining into. But it's absolutely true: you know there is an answer to this. Sometimes in programs that I did at 3M, you didn't know if there was an answer. You were going to try and make a thing that did this or that, but you didn't know that you were going to be able to do it. But if you want molecules that are useful, that are self-evidently very important, you can bet many human proteins including EPO are going to be important. You might not be smart enough to know that this could be a billion-dollar business. But you certainly are smart enough to know the thing is extremely important, and that is the driver. And you know it exists, so that's the driver.

[Tape 5, Side B]

Rathmann: The fact is, you always know there is that molecule. That's important, and that keeps you going. It was like that for EPO.

Hughes: What did you have to learn in running Amgen that you hadn't experienced before, and what did you get from Amgen that you hadn't gotten before?

Rathmann: You don't go through twenty-plus years of life in a research environment without experiencing a lot of important stuff. The thing that was different was the dependency on outside finances. That is not exactly black and white, because when you're at 3M, each year you go before the management, and you convince them of your budget. You know that you've got a job to do, and if they don't approve your budget, you have tough times. Still, in terms of the people that you're talking to, they understand you; they put you there in the first place, so they certainly have some obligation to help keep financing you. So it's really quite different from the biotech industry.

The idea that you're going to be totally dependent upon strangers to loosen up with their own private money to keep your company going is a shocking awareness. You're not without your negative examples very early. There was a subsidiary of Genentech; it was called Armos. They went under after the first five or six months of Amgen. There were just enough examples like that that floated to the surface. You watched companies die, and you'd think, wow, this is a different world. You can't ever get a chip on your shoulder: "I'm entitled to financing; the world owes me this." You get pretty humble.

As a matter of fact, I was extremely humble. In order to get visibility with potential investors, I would crawl and creep to their knee and say, "I want to be at your conference if I possibly could. You've got a wonderful conference, please let us in." Sometimes we got beat up because they didn't want you in because you weren't useful; you weren't a big enough company yet. So you learned that getting money is not only way, way up there in your priorities, but it's a difficult job. And unfortunately, you're subject to such violent changes that have nothing to do with you—the season, the cycle, whatever. Suddenly you have to face the reality that maybe six months ago, you would have done it this way, but now you're not going to do it that way. Right now, nobody wants to make an investment. Although as I look over my entire career starting with Amgen, I think the investment climate has been worse by substantial amounts in the last three or four years than it ever was. I don't remember it that bad before, but I remember it was still a learning experience, and one that I certainly had not been totally prepared for in my experience. Now, the second part to your question?

Hughes: The second part is, what did you get from Amgen that you hadn't gotten before in your career?

Rathmann: It's terrible to mention; I hate to talk about it, but personal recognition. When you're at Abbott Labs or 3M, you could be responsible for creating a one-hundred-million-dollar business, and probably nobody in the world will really know that. And it absolutely happened. You're not being burdened or anything; it's just that you don't feel that it's necessary to be recognized because you're part of an organization that's doing it. When you're a CEO of a new start-up, right or wrong, you're going to get the lion's share of the blame and the lion's share of the credit, and it's not a bad equation. It's fairly symmetrical. Things can go bad because of changes in the business climate, and you're a turkey. Things can go bad because a very good product had one flaw, and it failed, and you're a turkey. Those are tough pronouncements about the value of you as a human being. I watched some wonderful people get treated pretty badly at various times as a result of their downturns in the environment. So you have a sense of a totally different dimension in terms of leverage of your own personal career and your personal outlook. You can get pretty darn discouraged if you happen to hit a period like the last couple of years where it's very hard to raise money; it's very hard to get people to think that

you're a useful company. It's a tough life. I think I was somewhat hardened to this by some of my past experiences, like Litton.

I think that at Amgen, you feel a little bit like the Lone Ranger; that's a great spot, great horse. But you feel like there might not be anybody there if you need them. The reaction at Amgen where that was probably the clearest was that some of the people at Abbott had come out to see us and had drawn the conclusion, either by what I said or what I didn't say, that we were probably failing. During that time, they kind of passed the word around Abbott, which was a convenient thing to share, "George is really sorry he left Abbott. He bit off more than he can chew. It's really a tough thing these days. That's too bad because he's out there and it's tough." I didn't feel that way myself, so that's why I remember it. But I realized that it was probably a reading that people were getting from talking either to me or other people in the company: this isn't fun anymore. This is tough. I don't remember it being that bad, but I do remember the feedback from Abbott.

Hughes: And when did it change?

Rathmann: [pause] Well, it changed up and down. When you look at the public offering, we clocked it at about sixty days from when we got the final board approval to go public. We had sixty days of almost euphoria; you're going to go public; the value of the company is going to go to two hundred million dollars; stock options which we all had at one or two dollars a share are now worth eighteen dollars a share—it's a high. But when the stock got drubbed after going public, at its lowest low, you're worse off than you were before you became a public company. I think that changes of outlook were fairly frequent, but 1983 and '84 were certainly the most dramatic.

But when you suddenly have another company telling you that they own the EPO business, that's a downer beyond anything you can ever imagine. And your stock drops from forty dollars to twenty dollars in less than a week, and you've now lost your franchise. EPO is gone. The Genetics Institute's patent issues. So that's about as low as you can go. Then you come along and you're working, and you find yourself with a tremendous amount of talent working for you, and you think, I can't really ask for anything better than this. Some of the lawyers that we had were totally remarkable in this particular case, where we now had to beat Genetics Institute in the courtroom. When you suddenly find that you have enormous talent working on your side, you feel that you can do it, you can do it! Yet, any bad day, some of your arguments hit the wall and don't stick, and you get pretty discouraged with the case and the judge.

I watched the court case almost day by day for about six months. We had gone to the circuit court of appeals, federal circuit [United States Court of Appeals for the Federal Circuit]. Their decision took over a year. It arrived while I was running Icos. I got a call about seven o'clock at night from the top attorney at Amgen, saying, "You wouldn't believe this, George, but we got it all." "What do you mean, you got it all? How?" "The Court of Appeals for the Federal Circuit has taken our position with respect to both our patent and the G.I. [Genetics Institute] patent. We've been vindicated across the board." I said, "Well, is this a final decision?" He said, "Well, you never know, but it was a unanimous decision of the three judges that advocated for us." Well, then G.I. appealed the decision, meaning that all the judges in the court of appeals had to take a vote. That was unanimous in Amgen's favor. Then the people at G.I. took it to the Supreme Court to see if they could reverse the court of appeals decision. We start getting our story

ready for the Supreme Court, and they hire attorney Larry Tribe. Larry Tribe has a preeminent reputation for bringing cases to the Supreme Court, and his batting average is about 80 percent. Now the world says Amgen only has a 20 percent chance of winning this one. That wasn't true. We could win by never letting the Supreme Court decide they wanted to take this case, and that's what happened. So he's 80 percent when the Supreme Court decides to take the case, but he's batting zero when the Supreme Court passes it up. So the Supreme Court decided not to review the case, and all that weight dropped off our back.

Although gradually emerging as a better company and a stronger company with more recognition, we still had ups and downs that take you down pretty low. Of course, right along parallel with that is the story with the Johnson and Johnson, and that's a terrible story. It's a terrible thing to find yourself fighting motherhood, for gosh sake. Johnson and Johnson was really such a wonderful, pure, beautiful company, with the top ethics in the world and so on, and you're absolutely convinced they're scoundrels, and they're treating you very, very badly. They're supposed to be your partner, and that puts them in a great advantageous position to hurt you. They're getting your data, and then they're taking it to the FDA and saying, "Amgen's overdosing." They're taking advantage of the fact that we're partners. It was a really terrible experience, and that one's not over. I was talking to the attorneys about another lawsuit at Amgen, and they said they still have a feeling that there are additional chapters to be played in the J&J suit. So, it's a rollercoaster ride that takes extraordinary resilience. One of those dips is going to get you feeling pretty horrible. But, you remember the fact that you got through that one.

There are similar stories. The Icos story had similar events. We would think that we had our problems all behind us, and then would run into a big one, and we would think that it was a black tunnel that was never going to change. What we gained from Amgen was the ability to deal with these kinds of problems a little better the next time, probably a little tougher the next time. I think each of these experiences is comforting. So when your partner starts to act up, you don't wait for him to literally cream you; you go after him right off the bat. When our partner at Icos started to act up, I took a very strong position. I had gotten some very good legal counsel before, and I went back to the attorney that I knew at Amgen, and he helped chart a strategy in which we came off very, very, very well.

The fortunate thing is that all of these things are learning experiences. Even some of the negative experiences are still learning experiences. Litton was a learning experience, but a very negative experience. Amgen was largely positive. And yet I've made some absolutely incredible blunders in the latest company that I've been with, sometimes by applying what I thought I'd learned. So, what I learned at Icos was, by gosh, if you're really up against it, put your own money on the line, and you can turn it around. You can change the worldview of your company and turn it around. It helps to have Bill Gates with you, but it was certainly what I learned there. I tried to do the same thing at the company I'm with now, and I just got buried as there were other issues that worked against us. It was not the right answer for this one. So, you have to not only learn a lot, but then you have to know how to apply it. I was not always so great at that.

Hughes: Well, I don't know if the world would agree, but anyway, I thank you.

[End of interview]

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